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RADIOLOGY

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The Roentgen Aspects of Necrotizing Renal Papillitis[1]

RICHARD E. OTTOMAN, M.D., JOHN H. WOODRUFF, Jr., M.D., STEFAN WILK, M.D., and FRANK ISAAC, M.D.

ACUTE necrosis of the renal papillae occurs most frequently as a complication in patients with diabetes mellitus and acute pyelonephritis (11, 12, 13). Less frequently it complicates the clinical picture of obstructive uropathy with superimposed infection (10, 16, 17, 20).

Because of the urgent measures necessary for treatment of papillary necrosis, it behooves the radiologist, as a consultant, to be aware of the clinical and laboratory findings as well as of the diverse pyelographic changes that may take place. This paper includes a review of the roentgen observations recorded in the literature and a presentation of 8 cases of our own in which pyelography was performed.

Acute necrosis of the renal papillae is known by a number of names: "necrotizing renal papillitis," "renal papillary necrosis," "renal medullary necrosis," "necrotizing papillitis renis," and "Günther's necrosis," among others.

Necrosis of the renal papillae was first reported by von Friedreich in 1877 (40). He described varying stages of papillary destruction, including complete separation of the papilla, in a seventy-year old, nondiabetic male suffering from obstructive uropathy.

From 1877 to 1937, only occasional accounts appeared in the literature. In 1937, Günther emphasized the frequent association of diabetes mellitus with papillary necrosis (11, 12). In addition, he was probably the first to appreciate the full significance of the pyelographic changes to be observed.

Since 1937, reports of this important complication, which is found in 3 to 5 per cent of diabetics at autopsy (2, 4), have become increasingly frequent. Only an occasional publication, however, has appeared in the roentgenologic literature (5, 21).

CLINICAL FINDINGS

Although a few cases have been recorded in which the occurrence of necrotizing renal papillitis was recognized in the patient's lifetime, the diagnosis is still usually established postmortem. This is because the onset of papillary necrosis is obscured by the more prominent signs and symptoms of the primary disease: usually diabetes mellitus, becoming uncontrollable, or progressive obstructive uropathy and, in either case, superimposed upper urinary tract infection.

In the acute form of the condition, however, the urinary signs and symptoms become prominent with great rapidity, with costovertebral tenderness, pyuria, hematuria of varying degree, oliguria, azotemia, and prostration, proceeding to uremic coma and death.

[1] From the Departments of Radiology, University of California Medical School, Los Angeles, Harbor General Hospital, Torrance, and Long Beach Veterans Hospital, Long Beach, Calif. Presented at the Forty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 11–16, 1955.

A smaller group of patients with either known or unsuspected chronic pyelonephritis may have a prolonged subacute course. Episodes of exacerbation are followed by remissions. Exacerbations may be related to heightened activity of the chronic pyelonephritis or to isolated episodes of papillary necrosis. In the latter instance spasmodic renal colic may occur, as a result of obstruction of a major calyx or ureter by the sloughed papillae. Eventually, one of the flare-ups becomes more severe and the patient enters the acute phase.

A small number of cases have been reported in which both diabetes mellitus and obstructive uropathy were absent (3, 9, 30). In such cases an increasingly severe upper urinary tract infection develops, eventually ending in papillary necrosis. The clinical transition from an ordinary urinary infection to necrotizing renal papillitis, in these instances, still remains obscure.

The onset of complicating papillary necrosis should be suspected in any patient with diabetes mellitus or obstructive uropathy whose clinical condition suddenly becomes worse and in whom there is a decrease in urinary function and a rapid rise in the blood urea nitrogen. Laboratory findings are usually microscopic to gross hematuria, albuminuria, glycosuria in the diabetics, bacilluria, frequently decreasing urinary function (1), and a rising blood urea nitrogen or non-protein nitrogen (19).

ROENTGENOLOGIC FINDINGS

The roentgen appearance of papillary or medullary necrosis varies. It is best understood in relation to the type and degree of destruction occurring within the papilla or pyramid. Any changes resulting in loss of mucosal continuity over the papillae can be expected to alter the pyelographic appearance of the calyceal fornices or the papillae, thereby distorting the calyceal outline. Any necrosis which occurs *without* loss of mucosal continuity will result in essentially negative pyelographic findings. While these changes have been demonstrated by excretory urography, the decreasing renal function and the progressive azotemia make reliance upon retrograde pyelograms preferable.

Some authors have indicated a difference between papillary and medullary necrosis, depending upon the major site of initial necrotic change. Superimposed upon the findings of papillary or medullary necrosis are those of the accompanying infection, acute or chronic pyelonephritis, if their changes be anatomically manifest.

Papillary Necrosis (Fig. 1): The earliest identifiable change in papillary necrosis is little more than minimal deformity in the calyceal fornix around the affected papilla. This may be no more than is consistent with chronic pyelonephritis or may be sufficient to change the normal sharp calyceal outline to a hazy indistinct border. Next, with increasing severity of the accompanying infection, the calyceal fornices and the infundibula may become narrower (Cases I, II, and V).

When sequestration of the involved papilla begins, the contrast medium penetrates into the necrotic substance and presents on the pyelograms as ragged channels or sinuses. As the sequestration becomes more and more complete, the roentgen finding changes progressively from a small sinus to an "arc," and eventually to a "ring" (1) shadow (Case IV, right kidney), with the sloughed papilla lying virtually free in the minor calyx. Once the freed papilla has been extruded into the renal pelvis, there remains a large roughened cavity which is irregularly flattened on the cortical side at the site of the sequestration (Case III). This cavity fills easily with opaque material during retrograde pyelography. At this time the extruded papilla may be free in the pelvis or ureter, giving (Case VI) the appearance of an angular lucent defect within the contrast medium. In the ureter, it may be large enough to obstruct the free flow of urine (Case VI), resulting in proximal dilatation and symptoms of ureteral colic (18).

Medullary Necrosis (Fig. 2): According to Günther (12), if the necrosis is deep within the pyramid, the process will not be recognized until the tip of the papilla is disrupted. This disruption of mucosal continuity gives rise first to small fistulas, accompanying edema may result in elongation and distortion of the calyces, infundibular narrowing, calyceal amputation, and renal enlargement. These signs may be sufficient to suggest an infiltrating tumor pyelographically.

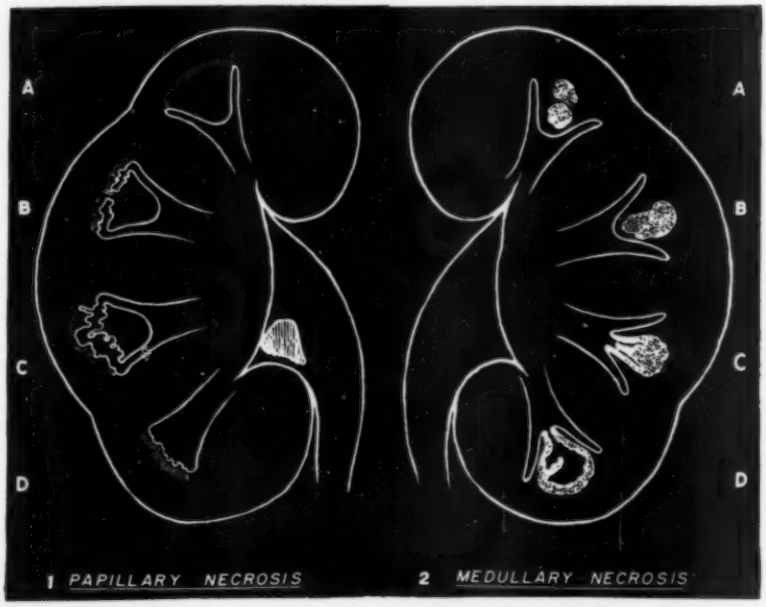

Fig. 1. Papillary necrosis. A. No interruption of papillary mucosa nor beginning sequestration. Pyelograms negative at this stage. B. Sinus tract formation allowing medium to penetrate into papilla; initial stage of sequestration. C. "Ring shadow" after complete papillary sequestration. D. Sloughed papilla has been extruded from calyx, leaving a small cavity flattened on the cortical side.

Fig. 2. Medullary necrosis. A. Small segments of medullary necrosis; papillary mucosa not compromised. Pyelograms negative at this time. B. Areas of necrosis coalesce. Still no pyelographic change. C. Mucosa over papillary tip disrupted, with extrusion of part of necrotic debris. Pyelograms show irregular channeling or sinuses. D. As extrusion of necrotic debris continues, pyelographic changes indicate cavitation of pyramids.

Modified from Günther (12).

which may be confused with pyelocanalicular reflux on the pyelogram. As the necrotic tissue is extruded into the kidney pelvis, the fistulas enlarge (Case VII), communicate with the pyramid, and form a small cavity (Case II, left) within it. When solitary, this cavity with communicating sinuses (Case VIII, left kidney) may simulate the pyelographic appearance of certain specific ulcerative granulomas, such as renal tuberculosis or actinomycosis, or may even suggest a calyceal diverticulum.

As the necrosis spreads, involving many or all of the papillae, the inflammation and

The numerous roentgen findings observed in our 8 cases of necrotizing renal papillitis are as follows:

1. Calyceal haziness or unsharpness.
2. Ulcerative or erosive papillary changes.
3. Sinus formation:
   (*a*) Intramedullary.
   (*b*) Intrapapillary (ring shadow).
4. Parenchymal cavitation with communicating sinuses.
5. Amputated calyces.
6. Extruded papilla with secondary
   (*a*) Club-like papillary fossa.
   (*b*) Ureteral or calyceal obstruction.
   (*c*) Intra-pelvic filling defect.

Fig. 3. Case I. Sixty-one-year-old white male with long history of progressive multiple sclerosis leading to paraplegia, obstructive uropathy with dysuria and frequency, and bladder calculi. Revision of vesical neck failed to produce adequate improvement of obstructive symptoms. Death in uremia with NPN at 160 mg. per cent.

A and B. *Right and left pyelograms of May 26, 1945,* showing no evidence of papillary necrotic changes. Reproduced for comparison with those of Dec. 1, 1948, obtained just before the patient's death.

C. *Right pyelogram, Dec. 1, 1948,* just before death, showing the following changes of papillary necrosis: (1) The inferior major calyx is now very slender, and its calyces are not identifiable. (2) The middle calyces are grossly distorted and indistinct, with an irregular, moth-eaten outline. (3) The superior calyx is likewise unsharp and ragged, due to fine, radiating sinuses extending from the calyx.

D. *Left pyelogram, Dec. 1, 1948,* showing the following changes: (1) The inferior calyces are irregular, with narrower fornices. The upper minor calyx has a club-like configuration compatible with complete separation of the papilla. (2) The middle calyx shows a narrower fornix, with one small superior projection of contrast medium. (3) The superior calyces are distorted, with irregular outlines, and communicate with one or more small sinus tracts. Erosion of the papilla is demonstrated in the medial calyx.

7. Narrow infundibula, occasionally showing a "moth-eaten" margin.
8. Decreased urinary function as seen on the intravenous pyelogram.
9. Enlargement of the renal silhouette.

DIAGNOSIS

A diagnosis of necrotizing renal papillitis may be made accurately by retrograde pyelography, particularly if attention is paid to the findings indicated above and to the clinical history of the patient.

The condition may also be diagnosed by histologic examination of bits of a sloughed papilla passed in the urine or lodged in the bladder and recovered during cystoscopy, as in Case IV (14). The microscopic appearance is that of an ischemic infarct with associated inflammatory changes of acute ascending pyelonephritis (15). Within the necrotic tissue there is loss of cell detail, but the basic architecture of the renal papilla remains. Any

inflammatory cells present are round cells, predominantly plasma cells (8).

DIFFERENTIAL DIAGNOSIS

While the pyelograms may at varying stages simulate those of other disease processes, the clinical examination permits a decisive interpretation.

At this point, the retrograde pyelograms may prove confusing. Close study of the entire urinary tract will disclose no evidence of involvement of either the renal pelvis or ureter in papillary necrosis, while in renal tuberculosis such involvement is common. Careful culture of the catheterized urine specimen will reveal

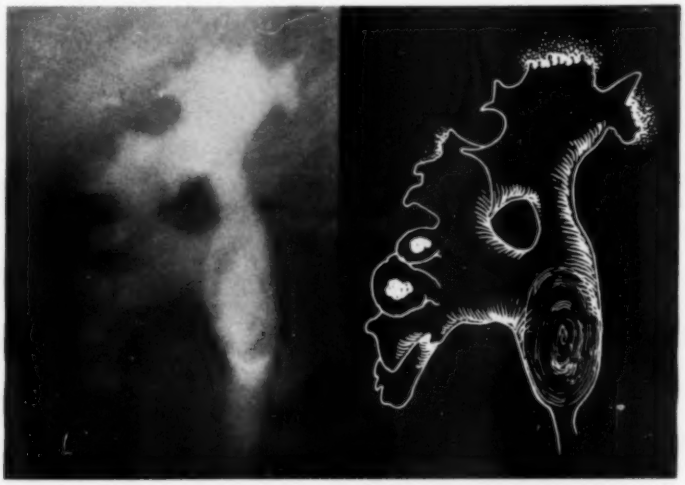

Fig. 4. Case II. Sixty-one-year-old white male with a long history of steadily progressive paralysis agitans leading to complete deterioration.
Excretory urogram shows a large opaque calculus at the ureteropelvic junction on the right. Mild dilatation of calyces. Mild irregularity and lack of clear definition of calyceal and papillary outline.
Bilateral pyelonephritis; right ureteropelvic calculus; right hydronephrosis and necrotizing papillitis.

Pyelocanalicular backflow occurs in normal kidneys; it is not infrequent and can be seen in retrograde and, occasionally, in intravenous pyelograms. The papillary tip appears smooth in outline; the contrast medium penetrates several millimeters into the tubules, which fan out from the apex of the papilla in a symmetrical manner. Several of the tubules are usually visualized simultaneously in one or more papillae. Pyelocanalicular backflow, *per se*, is not accompanied by the decreasing urinary function, rising azotemia, and prostration seen in necrotizing renal papillitis.

Renal tuberculosis is a specific inflammation leading to caseation necrosis, which may ulcerate a papilla and, in turn, produce a small cavity as well as sinuses. the acid-fast bacillus. Renal parenchymal calcification may frequently be found. A routine chest film is also of aid in indicating the presence of tuberculosis.

In *acute pyelonephritis without necrosis* the papillary tip is found intact. The major roentgen changes are in the calyces and infundibula. The clinical picture is less severe, and the patient responds to conservative therapeutic measures.

Stones in the urinary tract are radiolucent in 1 to 2 per cent of cases. This possibility must be borne in mind in investigation of renal colic. These stones, composed usually of uric acid or cystine, are round or oval in configuration. The sloughed papilla tends to be angular and, if multiple views are obtained, this appearance, due to the manner of sloughing, can be demon-

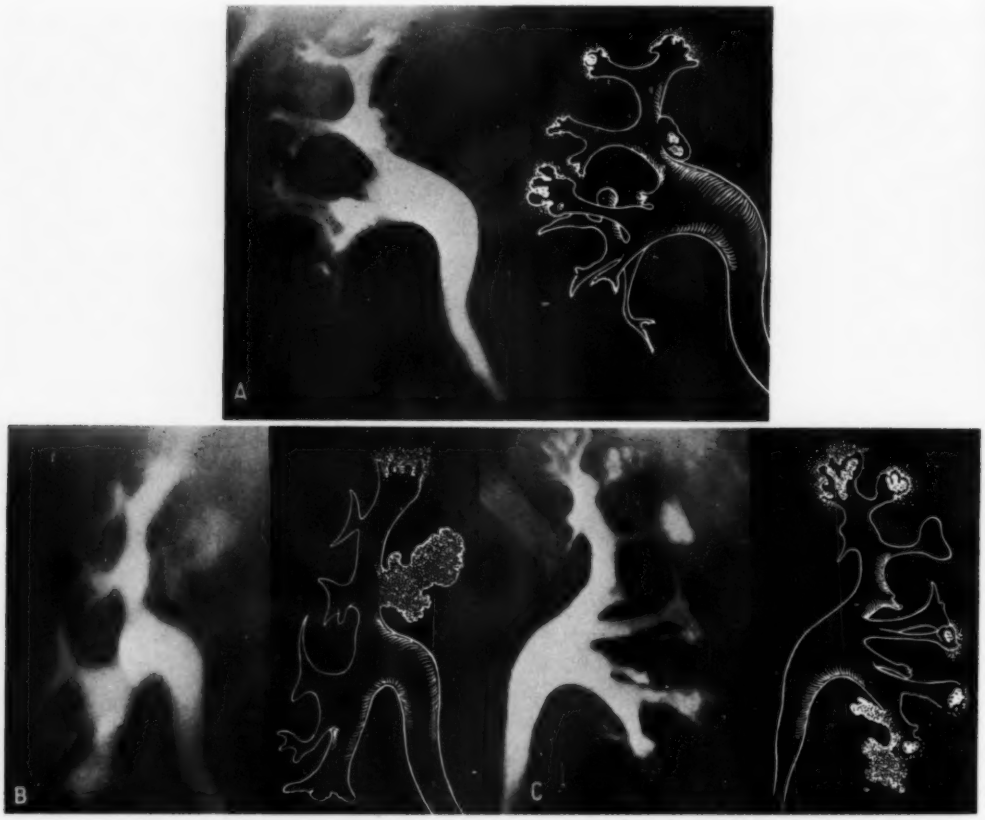

Fig. 5. Case III. The patient entered the hospital complaining of left costovertebral pain. He was a known diabetic whose pyelonephritis began to go out of control two weeks before admission. During hospitalization right flank pain and gross hematuria developed. Later the patient became comatose and died.

Necrotizing renal papillitis; diabetes mellitus; suppurative pyelonephritis.

Anteroposterior (A) and oblique (B) views of right and anteroposterior view (C) of left kidney, showing (1) distorted, indistinct and irregular calyces consistent with erosive changes in calyx and adjacent structures; (2) intramedullary and intrapapillary sinus tracts, some of which communicate with parenchymal excavations; (3) infundibular stumps without calyceal visualization; (4) narrowed infundibula, at times with irregular margins; (5) club-like calyces due to extrusion of sloughed papilla.

strated. Examination of the renal calyceal system in the case of a lucent stone (or blood clot) will not reveal absence of the papilla; this is not true with a sloughed papilla. Examination of the material passed during renal or ureteral colic will differentiate the lucent stone, the blood clot, or the sloughed papilla as the offending agent.

Neoplasms of the kidney may on occasion cause distortion of a portion of the calyceal system, usually with encroachment upon the pelvis. They begin, as a rule, in one of the kidney poles. As the tumor grows, more and more calyceal and pelvic distortion results. In papillary necrosis, the pelvis is not directly involved. In the generalized form of the disease, however, the calyces are found in varying degrees of distortion; the process is usually bilateral, and the patient is severely ill, bordering on uremic coma.

DISCUSSION

Roentgenologic procedures for the investigation of papillary necrosis include the following:

The routine *supine film of the abdomen* will show enlarged renal outlines which, however, may also be seen in lupus eryth-

Fig. 6. Case IV. Seventy-two-year-old Mexican male with history of chronic vomiting and hiccoughing and diarrhea for one week. He was in uremia, with a BUN of 70 mg. per cent. During a previous admission a specimen of necrotic renal papilla was obtained from the bladder during cystoscopy.

Necrotizing renal papillitis; diabetes mellitus.

A. *Right retrograde pyelogram, June 9, 1955,* showing: (1) narrowed, indistinct superior infundibulum with sinus tract formation; (2) "ring shadow" at superior calyx, consistent with beginning papillary extrusion. (3) irregular haziness along margins of other calyces.

B. *Left retrograde pyelogram, June 8, 1955,* showing (1) irregularity and poor definition of the superior calyces consistent with papillary erosions; (2) hazy outlines of other calyces.

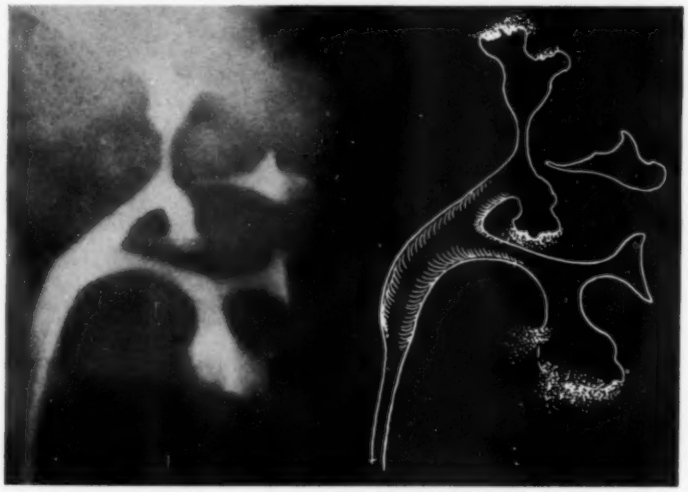

Fig. 7. Case V. Seventy-two-year-old white male admitted with congestive heart failure and coronary insufficiency. Progressive elevation of NPN occurred during the terminal period. Additional findings were a saccular aneurysm of the ascending aorta, and undifferentiated carcinoma of the lung.

The *left pyelogram* shows indistinct, irregular calyces consistent with papillary erosion. Similar findings were present on the right.

Pyelonephritis, acute and chronic, with necrotizing papillitis; nephrocalcinosis.

ematosus disseminatus, acute pyelonephritis, renal tumor, and polycystic kidney disease.

The value of the *excretory urogram* is limited, because of the poor renal function associated with papillary necrosis, but the process has been demonstrated with the aid of adequate lower abdominal compression (39).

Retrograde pyelography is the method of choice (1, 11, 12). This procedure can be best relied upon to fill any fistulas or

Fig. 8. Case VI. Seventy-one-year-old white diabetic female with episodes of left renal colic with fever and chills. Cystoscopy and ureteral catheterization revealed obstruction in lower third of left ureter. Tumor or a non-opaque stone was considered. The patient also had pyuria (left), hematuria, albuminuria, glycosuria, and a BUN of 38 mg. per cent. Surgery was cancelled because of pneumonitis. The patient was still living with disease three months after these studies.

Clinical diagnosis: Left pyonephrosis; right chronic pyelonephritis; necrotizing renal papillitis.

A. *Retrograde pyelogram, lower ureter, March 4, 1955.* Filling defect in lower third on left. Ureteral defect consistent with sloughed necrotic papilla *en route* to bladder. (No obstruction on later pyelogram.)

B. *Left pyelogram, March 4, 1955,* showing severe pyelectasis and caliectasis; club-like deformities of calyces; intrapapillary and intramedullary sinus tracts.

C. *Repeat left pyelogram, March 14, 1955.* Note lack of pyelectasis. No obstruction in lower ureter at this time. Marked irregularity and deformity of all calyces, some club-like. Pelvis consistent with sloughed papilla.

channels and demonstrate the degree of cavitation or sequestration. As bland an opaque medium as possible should be used, with only low-grade pressure, in filling the urinary tract, so as not to precipitate necrosis within inflamed papillae (5, 6).

In 8 of 15 cases reviewed, pyelographic studies were done: 7 had significant retrograde pyelograms or pyelograms obtained through nephrostomy tubes, demonstrating varying degrees of papillary and medullary necrosis and only moderate chronic pyelonephritis; in the eighth an intravenous pyelogram showed evidence of unilateral papillary necrosis. Five of the 8 cases studied were identified at autopsy and the pyelograms were found to be significant in retrospect. One case was diagnosed by pyelography and recovery of a sloughed papilla during cystoscopy. In 2 the diagnosis was made by pyelography in association with the clinical course. Details of the 8 cases are given in Table I.

TABLE I: EIGHT CASES OF NECROTIZING RENAL PAPILLITIS

Patient	Age	Sex	Basic Renal Disease	Associated Major Diseases	Proof
Case I	61	M	Right ureteropelvic calculus Right hydronephrosis Bilateral pyelonephritis	Debilitating paralysis agitans Prostatic hyperplasia	Autopsy Intravenous pyelograms
Case II	61	M	Acute and chronic pyelonephritis	Obstructive uropathy Multiple sclerosis with paraplegia; uremia	Autopsy Retrograde pyelograms
Case III	60	M	Suppurative pyelonephritis	Diabetes mellitus Acute bronchiolitis	Autopsy Retrograde pyelograms
Case IV	72	M	Chronic pyelonephritis	Diabetes mellitus Arteriosclerotic heart disease	Histologic examination of passed tissue Retrograde pyelograms
Case V	72	M	Acute and chronic pyelonephritis Nephrocalcinosis	Obstructive uropathy Arteriosclerotic heart disease with progressive congestive failure	Autopsy Retrograde pyelograms
Case VI	71	F	Chronic pyelonephritis	Diabetes mellitus Mild uremia	Suspected clinically Retrograde pyelograms
Case VII	56	F	Chronic pyelonephritis	Diabetes mellitus Low grade uremia	Suspected clinically Retrograde pyelograms Died in uremia
Case VIII	71	M	Hydronephrosis, left Suppurative pyelonephritis, right Bilateral hydroureter Chronic pyelonephritis	Adenocarcinoma of prostate with invasion of bladder and perivesical tissue Obstructive uropathy	Autopsy Injection of nephrostomy tubes

CONCLUSIONS

1. The roentgen appearance of papillary or medullary necrosis depends upon the type and degree of papillary destruction and sequestration.

2. This pathologic process occurs most frequently in patients with diabetes mellitus, less frequently in those with obstructive uropathy. In both groups there is an associated acute pyelonephritis.

3. The diagnosis may be made with a significant degree of accuracy by retrograde pyelography, and more exactly by histologic examination of portions of the sloughed papilla either passed in the urine or found in the bladder in the course of cystoscopy.

4. Earlier and more frequent recognition of this complicating process may permit more prompt institution of appropriate therapeutic procedures, with greater prolongation of life.

NOTE: Grateful acknowledgment is made to Ada Wing for her photographic aid and to Ted Bloodheart for his illustrations.

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BIBLIOGRAPHY

1. ALKEN, C. E.: Die Papillennekrose. Ztschr. f. Urol. **32**: 433–438, 1938.

2. AYE, R. C.: Renal Papillary Necrosis. Diabetes **3**: 124–128, March-April 1954.

3. DAVSON, J., AND LANGLEY, F. A.: Papillitis renis necroticans. J. Path. & Bact. **56**: 327–333, July 1944.

4. EDMONDSON, H. A., MARTIN, H. E., AND EVANS, N. G.: Necrosis of Renal Papillae and Acute Pyelonephritis in Diabetes Mellitus. Arch. Int. Med. **79**: 148–175, February 1947.

5. ESKELUND, V.: Necrosis of Renal Papillae Following Retrograde Pyelography. Acta radiol. **26**: 548–554, 1945.

6. FOULON, P., AND BUSSER, F.: À propos des lésions rénales secondaires à la pyélographie rétrograde. Ann. d'anat. path. **11**: 416–418, April 1934.

7. FROBOESE, C.: Über sequestrierende Marknekrosen der Nieren bei Diabetes mellitus. Verhandl. d. deutsch. Gesellsch. f. inn. Med. **30**: 431–443, 1937.

8. GAUSTAD, V., AND HERTZBERG, J.: Acute Necrosis of the Renal Papillae in Pyelonephritis; Particularly in Diabetics. Acta med. scandinav. **136**: 331–342, 1950.

9. GLUSHIEN, A. S., REITER, M. D., AND FISCHER, H.: Coronary Embolism (Intra Vitam Diagnosis) and Necrotizing Renal Papillitis. Case Report. Ann. Int. Med. **36**: 679–685, February 1952.

10. GRAUHAN, M.: Über die Entstehung von Pyonephrosen und entzündlichen Nierennekrosen. Ztschr. f. Urol. **28**: 462–472, 1934.

11. GÜNTHER, G. W.: Die Papillennekrosen der Niere bei Diabetes. München. med. Wchnschr. **84**: 1695–1699, Oct. 22, 1937.

12. GÜNTHER, G. W.: Die Mark- und Papillennekrosen der Niere, Pyelonephritis und Diabetes. Ztschr. f. Urol. **41**: 310–344, 1948.

13. HARRISON, J. H., AND BAILEY, O. T.: Significance of Necrotizing Pyelonephritis in Diabetes Mellitus. J.A.M.A. **118**: 15–20, Jan. 3, 1942.

14. JOHNSTON, D. H.: Repeated Bouts of Renal Papillary Necrosis Diagnosed by Examination of Voided Tissue. Arch. Int. Med. **90**: 711–717, November 1952.
15. KNUTSEN, A., JENNINGS, E., BRINES, O. A., AND AXELROD, A.: Renal Papillary Necrosis. Am. J. Clin. Path. **22**: 327–336, April 1952.
16. MANDEL, E. E.: Renal Medullary Necrosis. Arch. Int. Med. **91**: 417–418, April 1953.
17. MANDEL, E. E.: Renal Medullary Necrosis. Am. J. Med. **13**: 322–327, September 1952.
18. MELLGREN, J., AND REDELL, G.: Zur Pathologie und Klinik der Papillitis necroticans renalis. Acta chir. scandinav. **84**: 439–457, 1941.
19. MOREAU, R., DEUIL, R., CROSNIER, J., BLATRIX, C., AND THIBAULT, P.: Nécrose papillaire rénale au cours du diabète. Presse méd. **62**: 599–600, April 21, 1954.
20. MUIRHEAD, E. E., VANATTA, J., AND GROLLMAN, A.: Papillary Necrosis of the Kidney. Clinical and Experimental Correlation. J.A.M.A. **142**: 627–631, March 4, 1950.
21. OLSSON, O.: Spontanes Gaspyelogramm. Acta radiol. **20**: 578–584, 1939.
22. OVERZIER, C.: Ausheilung einer Papillennekrose der Niere. Virchows Arch. f. path. Anat. **309**: 600–606, 1942.
23. PACKARD, D. R., BEAZLIE, F. S., JR., AND CREECY, A. A.: Unusual Complications in Diabetes Mellitus. Case Report. Virginia M. Monthly **80**: 557–559, October 1953.
24. PELLEGRIN, F. A.: Necrotizing Renal Papillitis: Report of Case with Cystitis Emphysematosa and Intercapillary Glomerulofibrosis. Permanente Found. Bull. **5**: 66–74, July 1947.
25. PRAETORIUS: Papillitis necroticans bei schwerer chronischer Pyelonephritis. Ztschr. f. Urol. **31**: 298–299, 1937.
26. RICHFIELD, D. F.: Chronic Interstitial Pancreatitis with Diabetes Mellitus and Terminal Necrotizing Renal Papillitis. Ohio State M. J. **44**: 59–60, January 1948.
27. ROBBINS, E. D., AND ANGRIST, A.: Necrosis of the Renal Papillae. Ann. Int. Med. **31**: 773–793, November 1949.
28. ROBBINS, S. L., MALLORY, G. K., AND KINNEY, T. D.: Necrotizing Renal Papillitis: A Form of Acute Pyelonephritis. New England J. Med. **235**: 885–893, Dec. 19, 1946.
29. SWARTZ, D.: Renal Papillary Necrosis. J. Urol. **71**: 385–397, April 1954.
30. SHEEHAN, H. L.: Medullary Necrosis of the Kidneys. Lancet **2**: 187–189, July 24, 1937.
31. SILBERSTEIN, J. S., AND PAUGH, J. T.: Necrotizing Renal Papillitis. Ann. Int. Med. **38**: 689–705, April 1953.
32. SLIPYAN, A., AND BARLAND, S.: Renal Papillary Necrosis: Case Report. J. Urol. **68**: 430–436, August 1952.
33. STEVENS, R. J., WERTHAMMER, S., AND PEARSON, J. S.: Renal Papillary Necrosis Complicating Diabetes Mellitus. (Review of Literature with Case Report.) West Virginia M. J. **44**: 12–15, January 1948.
34. STOUDENSKY, A.: Über die Nierenpapillennekrose bei Hydronephrose. Ztschr. f. Heilk. **20**: 459–470, 1899.
35. THELEN, A.: Papillitis Necroticans bei chronischer Pyelonephritis. Ztschr. f. Urol. **40**: 67–76, 1947.
36. TURNER, F. C.: A Kidney from a Case of Phthisis, Showing Mortification of the Apices of the Pyramids. Tr. Path. Soc. London **36**: 268, 1884–1885.
37. TURNER, F. C.: Necrosis with Softening in Pyramids of the Kidneys: Recent Endopericarditis. Tr. Path. Soc. London **37**: 290, 1886.
38. TURNER, F. C.: Necrosis of Pyramids of One Kidney. Tr. Path. Soc. London **39**: 159–161, 1887–88.
39. VAN KEERBERGHEN, J., AND LEDERER, J.: La nécrose papillaire d'évolution chronique chez le diabétique. Presse méd. **60**: 1745–1747, Dec. 25, 1952.
40. VON FRIEDREICH, N.: Über Necrose der Nierenpapillen bei Hydronephrose. Virchows Arch. f. path. Anat. **69**: 308–312, 1877.
41. WALL, B.: Pyelographic Changes in Necrotizing Renal Papillitis. J. Urol. **72**: 1–5, July 1954.
42. WELCH, N. M., AND PRATHER, G. C.: Pneumonephrosis; A Complication of Necrotizing Pyelonephritis. J. Urol. **61**: 712–718, April 1949.

SUMARIO

El Aspecto Roentgenológico de la Papilitis Renal Necrotizante

Repásanse aquí los hallazgos roentgenológicos en la papilitis renal necrotizante, con la exposición de los hallazgos pielográficos en 8 casos.

Cabe hacer el diagnóstico con bastante precisión por medio de la pielografía retrógrada y, más exactamente, por el examen histológico de porciones de la papila esfacelada, expulsadas en la orina o encontradas en la vejiga durante la cistoscopia. El valor del urograma excretorio se considera limitado, debido a la deficiente función renal que acompaña a la necrosis papilar.

Las alteraciones pielográficas consisten en irregularidad de los cálices y cavernas renales, y varían de conformidad con la intensidad de la necrosis y la pérdida de tejido renal debida al esfacelo. Puede afectarse un solo riñón o pirámide, aunque el proceso es más a menudo generalizado y bilateral. La principal enfermedad que hay que considerar y excluir en el diagnóstico diferencial roentgenológico es la tuberculosis renal.

Las causas más comunes son, primero, diabetes azucarada, y segundo, uropatía oclusiva; ambas se asocian con pielonefritis aguda. Se ha descrito un pequeño número

de casos en que no existen diabetes o uropatía oclusiva, y en que el factor precipitante es una infección cada vez más grave de la porción superior del aparato urinario.

El reconocimiento más temprano y más frecuente de este proceso puede permitir la iniciación más rápida de apropiados procedimientos terapéuticos, con prolongación de la vida del enfermo.

Infantile Arteriosclerosis[1]

H. STEPHEN WEENS, M.D., and CARLOS A. MARIN, M.D.

CALCIFICATION and sclerosis of the arteries in infants and young children may be encountered in a variety of clinical conditions. Foremost among these are disorders in which disturbances of the calcium and phosphorus metabolism play an important role. Thus infantile arteriosclerosis has been recognized in renal disease (1), hyperparathyroidism, and vitamin D intoxication (2). Similar arterial changes have also been noted in progeria, in which the arteriosclerotic process is associated with extensive growth disturbances and profound metabolic changes (3).

Aside from these conditions, infantile arteriosclerosis has been observed in an increasing number of cases in which no obvious etiologic factors are apparent but which show considerable resemblance in their clinical manifestations and striking similarity in their pathologic findings. The principal morphologic changes of the arteries in these patients are a marked disorganization of the internal elastic membrane accompanied by deposition of lime salts in its proximity. Concurrently a marked fibroblastic proliferation of the intima takes place, which may attain such proportions that the involved vascular lumen becomes markedly narrowed or even obliterated.

The large majority of these cases have been discovered on necropsy and described in the pathologic or pediatric literature, where it has been repeatedly suggested that the arterial calcifications should be recognizable on radiologic examination. Unfortunately, radiologists are frequently unacquainted with this clinical entity, though the x-ray examination may well prove to be the most important means of establishing a diagnosis during life.

The following two case reports may illustrate the salient features of this condition.

CASE I: R. H., a colored male, was admitted at the age of ten months on account of progressive loss of weight and enlargement of the abdomen. The family history was not contributory. Delivery had been normal but neonatal weight gain had been poor.

The essential findings on physical examination were emaciation, abdominal distention, and a small umbilical hernia.

The radiologic examination of the chest was not remarkable. Roentgenograms of the long bones revealed a delicate but widespread calcification of the arteries which was most pronounced throughout the soft tissues of the forearm and lower extremities, where the blood vessels showed considerable tortuosity (Figs. 1 and 2). Vascular calcification could not be recognized throughout the abdomen, thorax, or skull

The laboratory findings, including serology, hemogram, blood chemistry, electrocardiogram, and duodenal trypsin activity were within normal range.

The blood pressure, determined by the flush method, was recorded as follows: Right arm, 170; left arm, 150; right leg, 180; left leg, 200. Repeated studies gave similar results.

After discharge and improvement, the child was readmitted at the age of sixteen months, with edema of the lower extremities. Emaciation and abdominal distention had considerably progressed. The blood pressure was now recorded as follows: Left arm, 120/82; right arm, 110/72. There was marked albuminuria, and the phenolsulfonphthalein test showed 75 per cent excretion in two hours. The blood urea nitrogen was 20 mg. per cent. In spite of supportive therapy, the patient died on the fifth hospital day.

Essential Autopsy Findings: The heart showed marked left ventricular hypertrophy and weighed 105 gm. (normal weight 48 gm.). Its appearance was otherwise not remarkable.

On *microscopic examination*, the medium-sized arteries of the heart showed a patchy calcification of the media, with intimal proliferation leading to diminution of the vascular lumina. Various degrees of fragmentation were noted in the internal elastic membrane of these vessels. The myocardial fibers were intact but separated from each other by moderate edema in the interstitial collagen.

Microscopic examination of the other viscera showed similar arterial changes, except that these

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changes were more pronounced in the spleen, pancreas, kidneys, adrenals, and thyroid (Fig. 3). In these organs the intimal proliferation of the vessels had often resulted in almost complete occlusion of the arteries. The lungs showed evidence of interstitial pneumonitis. The kidneys did not reveal any hemorrhages or exudates. The parathyroids were grossly and histologically normal.

The final *anatomic diagnosis* was medial calcification of the arteries of unknown pathogenesis,

Fig. 1. Case I. Extensive calcification of the arteries of the right arm.

Fig. 2. Case I. Tortuous pattern of arterial calcification. Contrast photographically increased.

left ventricular hypertrophy, pulmonary congestion and edema, and minimal interstitial pneumonitis.

Comment: This 16-month-old male infant died with widespread arteriosclerosis and marked cardiac hypertrophy after a prolonged period of failing health. The arterial calcification could be demonstrated radiologically during life. Hypertension was a remarkable clinical finding in this case. The etiology of the process remains obscure.

CASE II: R. L. L., a white male infant, on the fourth day of life experienced an episode of vomiting, fever, and rapid respiration. His delivery had been normal, and the family history was not remarkable. A spinal tap on the seventh day of life disclosed xanthochromic fluid under normal pressure. A

chest roentgenogram on the same day showed a patchy atelectasis of both lungs.

Three weeks after birth, the child was transferred to the Henrietta Egleston Hospital. His body was in opisthotonic position, and ptosis of the left eye was noted. The hemogram disclosed moderate anemia and slight leukocytosis.

Subdural tap and trephination of the skull confirmed the diagnosis of intracranial hemorrhage. Death occurred on the twenty-fifth day of life. There was subarachnoid and interventricular hemorrhage as well as hemorrhage into the temporal lobe.

On the basis of the autopsy findings, the roentgenograms of this patient were reviewed. On one chest film the upper extremities were sufficiently depicted to demonstrate extensive calcification of the arteries within the soft tissues of the upper arm and forearm (Figs. 5 and 6). The roentgenograms of the chest and abdomen did not disclose calcification of the visceral structures.

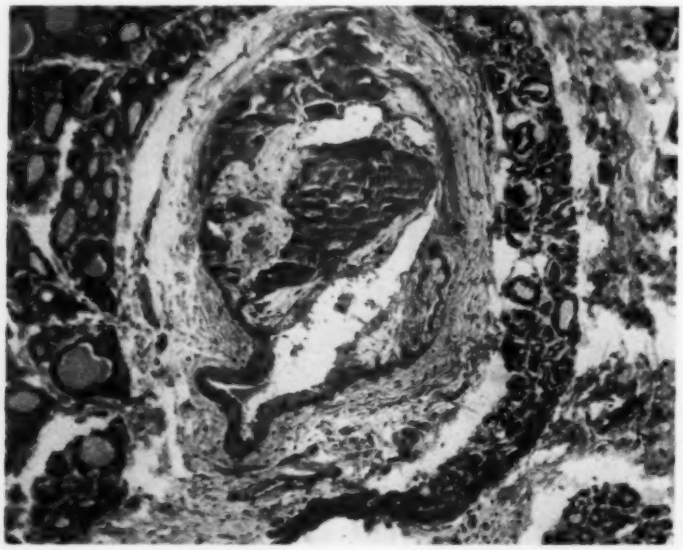

Fig. 3. Case I. Medium-sized artery in the thyroid near the capsule. The vessel wall is distorted in outline, with marked variation of its thickness. This is due to patches of intimal fibrosis with narrowing of the lumen and calcification of intima and media. The deposits of lime salts are seen as dark-staining areas with irregular outlines.

Essential Autopsy Observations: The left cardiac ventricle was found to be enlarged, and the heart weighed 37.5 gm. (normal weight 23 gm.). Microscopically the myocardium showed focal areas of scarring in the subendocardium and between the muscle bundles. Patchy areas of calcification were found in the media of the coronary arteries, associated with many interruptions of the internal elastic membrane. There was early fibroblastic proliferation of the intima, but this did not significantly diminish the lumen of these vessels.

A similar type of calcification was seen in the pulmonary arteries and the arteries of the pancreas, adrenals, kidneys, and thyroid (Fig. 4).

An unusual and unexplained focal necrosis of the liver was noted. In the upper pole of the left kidney was a recent infarct which seemed to be secondary to vascular calcification and occlusion of the adjacent arteries.

The brain did not show any arterial lesions.

Comment: The predominant cause of death in this patient appears to have been the intracranial hemorrhage. It remains conjectural to what extent the widespread arterial disease contributed to the intracranial complications and fatal outcome. The case serves, however, to show that the arterial changes may be demonstrated on the roentgenograms of the upper extremities.

DISCUSSION

Approximately 40 cases of infantile arteriosclerosis have been reported in the literature (4–26). This does not include case records with incomplete clinical and pathologic description or cases in which

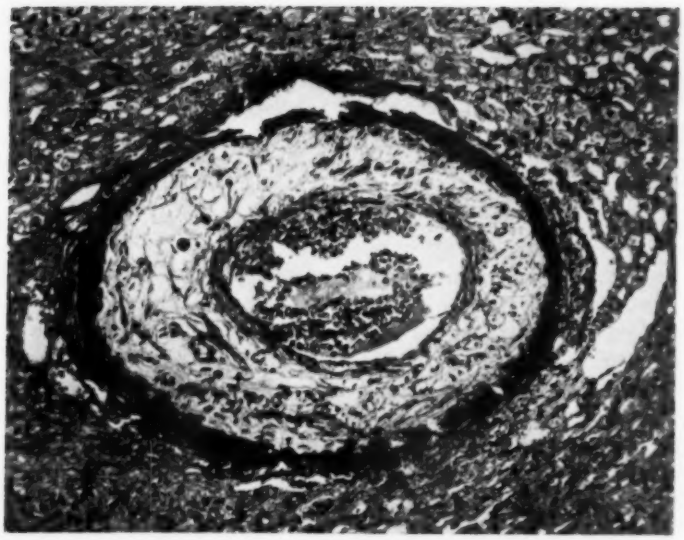

Fig. 4. Case II. Small artery of adrenal gland showing marked medial calcification associated with pronounced fibroblastic proliferation of the intima which has narrowed the vascular lumen.

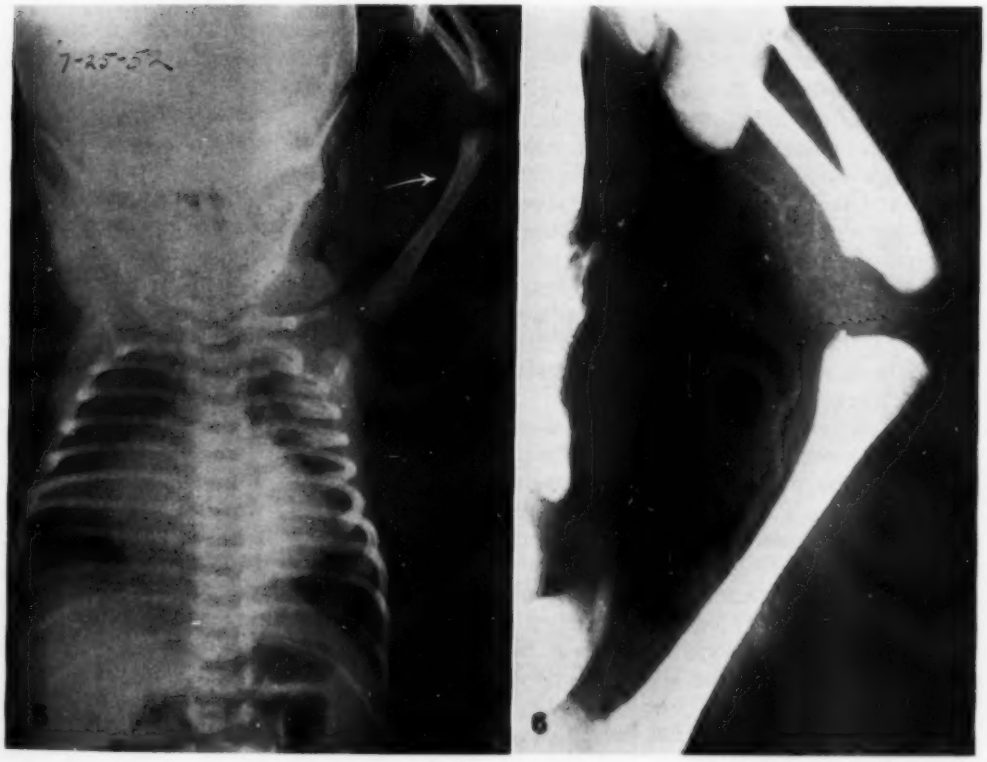

Fig. 5. Case II. Complete calcification of the arteries of the left arm. Patchy atelectasis and pneumonic infiltration in both lung fields.

Fig. 6. Case II. Marked deposition of calcium in the brachial artery and radio-ulnar branches. Contrast photographically increased.

such etiologic factors as vitamin D intoxication and advanced renal disease appear well established.

The pathologic changes of infantile arteriosclerosis seem to take place initially in the internal elastic membrane, which shows evidence of splitting and fragmentation, eventually leading to a complete disorganization. Associated with this process is a deposition of calcium salts which may extend deeply into the intima and media. A striking finding is the concurrent fibroblastic proliferation of the intima, which may markedly narrow or even completely occlude the blood vessel. On gross inspection, the involved arteries appear tortuous, as in instances of coronary artery involvement. Lipoid deposits are not observed in infantile arteriosclerosis, making it unlikely that those factors which are operative in the development of adult atherosclerosis play a significant role in the pathogenesis.

The similarity of the lesions described here to those occurring in derangements of calcium and phosphorus metabolism make an explanation for the arterial changes on a metabolic basis attractive. So far, clinical, pathologic, and laboratory observations have not afforded substantiation of such a concept. Possibly metabolic changes may occur which are so subtle that they have not been recognized, since there has usually been little opportunity to evaluate these patients carefully.

Recent pathologic and experimental studies have stressed the role of the elastic elements of the arteries in the development of arteriosclerosis (27). As histologic observations indicate that the incipient changes of infantile arteriosclerosis affect the internal elastic membrane, it is conceivable that a deficiency of elastic elements may, in itself or in association with extraneous factors, lead to the above described arterial changes (16).

Infantile arteriosclerosis has been proved to occur in siblings (19). The clinical history in several instances has shown that siblings have died under similar circumstances (9, 16). This observation makes it likely that genetic factors may predispose to the development of the condition.

The large majority of cases have occurred during the first year of life or in the neonatal period. In a large number of patients, particularly those with severe coronary artery disease, the onset of the symptoms was sudden, with development of cyanosis, dyspnea, and lethargy suggesting acute cardiac failure. In others, in whom there was a more subacute or chronic course, the clinical picture was largely that of impaired health with anorexia, vomiting, weight loss, and general debility. Cardiac enlargement and edema have been repeatedly observed, and in several instances electrocardiographic studies disclosed myocardial damage (22, 26). The presence of hypertension in Case I merits attention, though it is not possible at present to state that this should be considered as a causative factor or a result of this condition.

The coronary arteries, as well as arteries of the thoracic and abdominal viscera, are commonly affected, as well as the arteries supplying the extremities. A lack of cerebral arterial involvement in infantile arteriosclerosis is noteworthy. In general, the calcification observed roentgenologically does not differ from other types of arterial calcification, such as are encountered in advanced renal disease. The tortuosity of the vessels is frequently reflected in the corkscrew-like pattern of calcification.

The clinical symptomatology has usually not been sufficiently characteristic to permit a diagnosis of this disease entity, but the roentgen examination should make it possible to recognize the condition during life. In all cases of unexplained heart failure and cardiac enlargement in infancy and childhood, as well as in debilitating diseases of unknown etiology, calcification of the arteries should be searched for by proper radiologic studies.

Reviewing the literature, one is impressed by the paucity of cases in which there was the opportunity for adequate

clinical evaluation of these patients. It may be hoped that radiologic recognition of this condition during life will further the clinical investigation of infantile arteriosclerosis.

SUMMARY

1. Arterial calcification and sclerosis in infants may be encountered in a variety of metabolic disorders. Aside from these conditions, infantile arteriosclerosis has been observed in an increasing number of cases in which, at present, no obvious cause is established.

2. The pathologic changes in this type of arteriosclerosis consist of fragmentation of the internal elastic membrane, intimal and medial calcification, and fibroblastic proliferation of the intima. Arteries of medium size are predominantly affected. Clinical complications are caused by vascular occlusion.

3. Two cases are reported illustrating the pertinent clinical, radiologic, and pathologic features.

4. Etiologic factors are briefly considered.

5. Emphasis is placed upon radiologic examination as the most important means of establishing a diagnosis during life.

NOTE: We are indebted to Dr. M. Hines Roberts for clinical data on Case II.

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REFERENCES

1. PENDERGRASS, E. P., AND BROOKS, F. P.: Report of a Case of Osteonephropathy with Vascular Calcification in Infancy. Radiology **62**: 227–233, February 1954.

2. HUEPER, W. C.: The Etiology and the Causative Mechanism of Arteriosclerosis and Atheromatosis. Medicine **20**: 397–422, December 1941.

3. TALBOT, N. B., BUTLER, A. M., PRATT, E. L., MACLACHLAN, E. A., AND TANNHEIMER, J.: Progeria; Clinical, Metabolic and Pathologic Studies on Patient. Am. J. Dis. Child **69**: 267–279, May 1945.

4. DURANTE, G.: Cited by Oppenheimer (8).

5. JAFFE, R.: Cited by Oppenheimer (8).

6. SURBECK, K.: Cited by Oppenheimer (8).

7. HUGHES, F. W. T., AND PERRY, C. B.: Senile Arterial Changes in a Child Aged 7 Weeks. Bristol Med.-Chir. J. **46**: 219–222, 1929.

8. OPPENHEIMER, E. H.: Partial Atresia of the Main Branches of the Pulmonary Artery Occurring in Infancy and Accompanied by Calcification of the Pulmonary Artery and Aorta. Bull. Johns Hopkins Hosp. **63**: 261–277, October 1938.

9. FORRER, H.: Ausgedehnte Gefässverkalkung im frühen Kindesalter. Inaugural Dissertation, Zurich, 1930.

10. SCHEIDEGGER, S.: Cited by Muth (24).

11. VAN CREVELD, S.: Coronary Calcification and Thrombosis in Infant. Ann. paediat. **157**: 84–92, 1941.

12. BAGGENSTOSS, A. H., AND KEITH, H. M.: Calcification of the Arteries of an Infant. Report of a Case. J. Pediat. **18**: 95–102, January 1941.

13. BROWN, C. E., AND RICHTER, I. M.: Medial Coronary Sclerosis in Infancy. Arch. Path. **31**: 449–457, April 1941.

14. ANDERSEN, S. R.: Extensive Arterial Calcification and Cirrhosis of the Liver in a Newborn Infant. Acta. path. et microbiol. Scandinav. **22**: 180–187, 1945.

15. FIELD, M. H.: Medial Calcification of Arteries of Infants. Arch. Path. **42**: 607–618, December 1946.

16. STRYKER, W. A.: Arterial Calcification in Infancy with Special Reference to the Coronary Arteries. Am. J. Path. **22**: 1007–1031, September 1946.

17. DONAT, R.: Cited by Muth (24).

18. HAUSE, W. A., AND ANTELL, G. J.: Arteriosclerosis in Infancy. Arch. Path. **44**: 82–86, July 1947.

19. PRIOR, J. T., AND BERGSTROM, V. W.: Generalized Arterial Calcification in Infants. Am. J. Dis. Child. **76**: 91–101, July 1948.

20. MENTEN, M. L., AND FETTERMAN, G. H.: Coronary Sclerosis in Infancy; Report of 3 Autopsied Cases, 2 in Siblings. Am. J. Clin. Path. **18**: 805–810, October 1948.

21. LIPMAN, B. L., ROSENTHAL, I. M., AND LOWENBURG, H., JR.: Arteriosclerosis in Infancy. Am. J. Dis. Child. **82**: 561–566, November 1951.

22. MANT, A. K., TROUNCE, J. R., AND VULLIAMY, D. G.: Disease of the Coronary Arteries as a Cause of Death in Infancy and Childhood. Guy's Hosp. Rep. **101**: 115–125, 1952.

23. SLADDEN, R. A.: Coronary Arteriosclerosis and Calcification in Infancy. J. Clin. Path. **5**: 175–182, May 1952.

24. MUTH, S.: Zur Frage der Mediaverkalkung im frühen Kindesalter. Zentralbl. f. allg. Path. u path. Anat. **91**: 107–113, Dec. 19, 1953.

25. NESTOR, J. O., FOLSTON, M. J., AND HOWARD, W. A.: Arteriosclerotic Heart Disease in Infants. Clin. Proc. Child. Hosp., Wash. **9**: 10–25, January 1953.

26. COCHRANE, W. A., AND BOWDEN, D. H.: Calcification of the Arteries in Infancy and Childhood. Pediatrics **14**: 222–231, September 1954.

27. BLUMENTHAL, H. T., LANSING, A. I., AND WHEELER, P. A.: Calcification of Media of Human Aorta and Its Relation to Intimal Arteriosclerosis, Ageing and Disease. Am. J. Path. **20**: 665–687, July 1944.

(Para el sumario en español, véase la página siguiente.)

SUMARIO

Arteriosclerosis Infantil

En varios trastornos metabólicos, pueden observarse calcificación y esclerosis arteriales. Aparte de esas dolencias, se ha encontrado arteriosclerosis infantil en un número creciente de casos sin que se haya establecido hasta ahora una causa manifiesta.

En esta forma de arteriosclerosis, las alteraciones anatomopatológicas consisten en fragmentación de la membrana elástica interna, calcificación de las túnicas íntima y media y proliferación fibroplástica de la íntima. Se afectan predominantemente las arterias de tamaño mediano. Las complicaciones clínicas son provocadas por la oclusión vascular.

Se presentan 2 casos que ilustran las características clíncas, radiológicas y anatomopatológicas.

Se hace hincapié en el examen radiológico como medio más importante de establecer el diagnóstico durante la vida.

Total Unilateral Pulmonary Collapse

A Study of the Roentgen Appearance in the Lateral View[1]

MORTIMER LUBERT, M.D., and GEORGE R. KRAUSE, M.D.

THE PURPOSE OF this report is to attempt a complete analysis of the lateral roentgenogram of the chest in unilateral pulmonary collapse. Such an analysis should lead to a better understanding of the lateral view of the chest in general, and of the mechanism of unilateral pulmonary collapse in particular. Unilateral pulmonary collapse we define as "some loss in volume of an entire lung, with the component lobes contributing more or less equally to the total diminution in size."

Two approaches to the problem were selected. The first was a study of a number of cases, in most instances by serial roentgenograms of the chest. This permitted not only an analysis of the final picture but also of the steps through which the process evolves. The second approach consisted of an application of the roentgenologic principles inherent in the silhouette sign, as described by Felson (1), to the same series of cases and to others with related entities.

In some of our cases involvement of a lobar bronchus with lobar collapse preceded occlusion of a main bronchus and unilateral pulmonary collapse. The patterns of lobar collapse were those which we have previously described (2). Briefly, as seen in the lateral view, the right upper lobe moves upward and slightly forward; the left upper lobe moves forward and slightly upward; both lower lobes move downward and backward.

When a main bronchus to a lung becomes occluded, however, the result is a remarkably uniform end-pattern in the lateral view. (Space-compensation must come from outside the affected lung.) It makes no difference whether the process is on the right or the left, whether it begins in an upper, lower, or middle lobe, or whether the lung is involved uniformly from the start. The final pattern is basically the same, but the modifying factors which affect lobar collapse (2) must be remembered. Furthermore, when other processes, not primarily or solely endobronchial—such as constricting pleuritis and parenchymal fibrosis—cause a unilateral pulmonary collapse, the lateral view has essentially the same appearance as that resulting from a blocked bronchus (Fig. 6). As a matter of fact, even when the basic abnormality is obstructive emphysema of the opposite lung, with compression atelectasis of the normal, the appearance in the lateral view is still the same (Fig. 7).

The similarity in appearance is due to the action of similar forces on the same anatomical structures; it boils down to a net difference in pressure, between the two halves of the thorax, exerted on the mediastinum. The mediastinum, however, is a partition of differential mobility. Posteriorly it is more rigid, because of the vertebrae, esophagus, and descending aorta. In the middle mediastinum, which contains the trachea and the posterior portion of the heart, anchored by the venae cavae, there is more mobility. Anteriorly, there is only the free portion of the heart and the relatively thin tissue of the anterior superior mediastinum; this portion is most mobile.

Any difference in pressure between the two halves of the thorax would then exert its maximum effect anteriorly, with relatively little change posteriorly, and with gradation in between. The overdistended lung "herniates through" anteriorly, and the heart shifts to the side of lesser pressure. The trachea moves with

[1] From the Department of Radiology, Mt. Sinai Hospital of Cleveland, and the Radiologic Group of Drs. Mahrer, Krause, Lubert, Berman, and Bennett. Accepted for publication in August 1955.

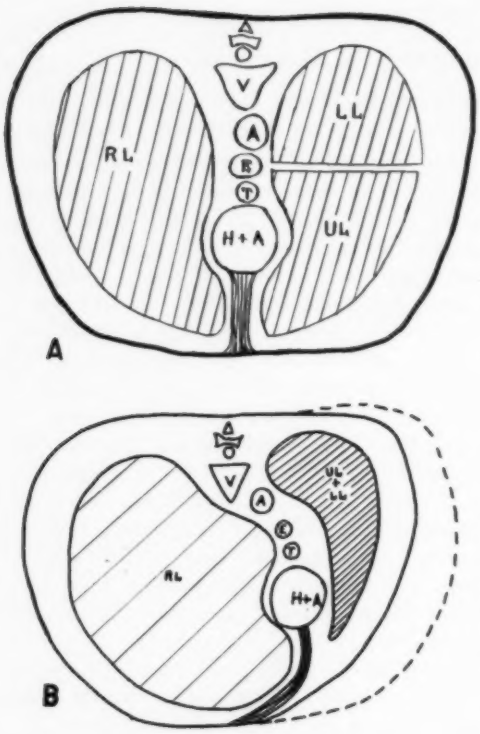

Fig. 1. Diagram of a horizontal section through the thorax at the level of the retrosternal space, seen from above.

A. Normal. V = vertebra; A = descending aorta; E = esophagus; T = trachea; H + A = heart and ascending aorta; RL = right lung; LL = left lower lobe; UL = left upper lobe. The anterior mediastinum is exaggerated in width but normal in position.

B. Same horizontal section in the presence of collapse of the left lung. The mediastinum is shifted to the left, anterior structures more than posterior ones. The expanding right lung fills the restrosternal space, accounting for the large radiolucent area seen on lateral roentgenograms. The expanding right lung also fills the retrocardiac space, but to lesser degree. It may even intrude between the structures of the posterior mediastinum (3). The left lung has moved laterally and posteriorly.

the heart. The lungs may also "herniate" through another unguarded area, the retrocardiac space, between the posterior border of the heart and the descending aorta. The descending aorta and esophagus move to a lesser extent and only when a greater effort is needed to compensate for lost lung volume on the involved side. Thus, the collapsed lung moves laterally, posteriorly, and inferiorly because maximum pressure is exerted anteriorly and superiorly. Figure 1 illustrates schematically the relationships in a horizontal section through the chest: A represents the normal; in B the differential mobility of the mediastinum is shown.

This sequence of events is responsible for the roentgen picture in total collapse of a lung. The appearance in the postero-anterior view is well known and need not be discussed here. The appearance in the lateral projection needs explanation.

APPEARANCE OF THE LATERAL ROENTGENOGRAM

If an entire lung collapsed uniformly and did not shift much in position, its greater density would have the effect of a relatively uniform filter applied over the entire lateral projection (Figs. 2, B and 5, C). Such a collapsed lung would not be identifiable clearly as a separate structure. In total pleural effusion there is also such a "filter" effect, as in Figure 9, where there is an overall graying of the entire roentgenogram. Unless the roentgen exposure is of sufficient penetration, the haze of this filter effect will obliterate all detail. If there is sufficient penetration, the structures of the normal side will show through (Fig. 5, C).

However, as has already been pointed out, the collapsed lung shifts posteriorly and inferiorly because of the differential mobility of the mediastinum. The opposite lung pushes the mobile anterior mediastinum ahead of it, occupies the retrosternal space, and thus causes an increase in its size and radiolucence. The heart and ascending aorta are displaced posteriorly by the "herniating" lung. When the collapse is on the left, the radiolucent space of the anterior mediastinum is somewhat larger than in right-sided collapse. This may be due to the position of the ascending aorta on the right.

In Figure 2, C we show schematically how the greater thickness of the collapsed lung posteriorly will cast a shadow on the lateral view (see also Figs. 3, D, 5, A, and 9, D). When part of the collapsed lung is also in contact with the opposite, over-

aerated lung tissue, which has pushed through the retrocardiac space, there will be an interface between this part of the collapsed lung and the lesser density of the opposite, over-expanded lung. Since this interface is tangential to the roentgen ray in the lateral view, a silhouette effect is created; part of the collapsed lung can thus be seen more easily in its postero-inferior position. This interface may simulate a pleural effusion posteriorly. When the collapsed lung is also airless and in contact with the homolateral diaphragm, the similarity of the densities will cause loss of the diaphragm shadow.

Whether the shadow of the arch and descending portions of the aorta will or will not be seen on the lateral view depends on physical factors. If they are engulfed by collapsed lung, pleural fluid, or pneumonic consolidation, they will not be seen because of the similar densities. They may be visible if they protrude into the aerated lung or are in contact with herniated lung tissue; there then will be an interface between two tissues of different density, tangential to the ray, so that a silhouette effect is created. When the collapse is on the left, the shadow of most of the arch and the descending aorta is usually hidden. The anterior margin of the ascending aorta is often obliterated in right-sided collapse.

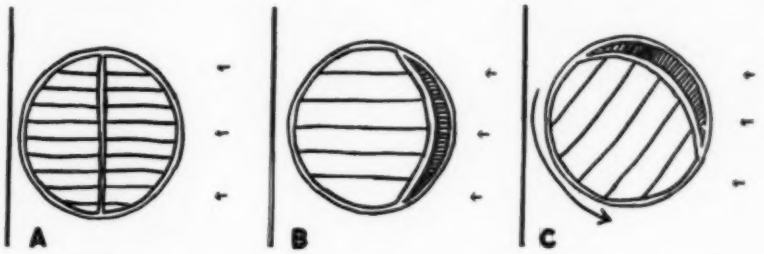

Fig. 2. Schematic representation of a section through the thorax seen from above, illustrating "uniform filter effect." The small arrows represent the direction of the roentgen ray in a lateral view.

A. Normal. Both lungs expanded. X-rays traverse a relatively fixed volume of aerated lung.

B. Collapse of a lung without rotation. Combined volume of both lungs is almost the same due to compensatory expansion of other lung. Collapsed lung, of relatively even thickness from front to back, acts as filter of uniform thickness at right angles to the roentgen ray. It will absorb x-rays and cause an overall "grayness" but casts no distinguishable shadow of its own. If penetration is sufficient, detail in the opposite lung will be seen. This uniform filter effect occurs in complete collapse when, for some reason such as mediastinal fixation or pleural adhesions, there is no significant rotation. It is also seen in complete consolidation and massive effusion (Fig. 5, C). The effect is the same as that obtained by placing a filter at the tube aperture.

C. Collapse with rotation. The combined volume of both lungs is still about the same as in B. However, relationship between collapsed and aerated lung has changed. Because the collapsed lung has rotated posteriorly (see Fig. 1, B), there is no filtration effect anteriorly. This, plus "herniation" of over-aerated, opposite lung, causes an anterior clear space. A greater portion of the collapsed lung is in the path of the roentgen ray posteriorly in the lateral view; also the ray is tangential to an interface between the collapsed lung and the oppôsite expanded lung, so that the shadow of a portion of the former can be seen more clearly (silhouette effect). See Figs. 3, D, 5, A, and 9, D.

PNEUMONIA AND PLEURAL EFFUSION

To this point we have discussed the dynamic changes which account for the appearance of the lateral roentgenogram in unilateral pulmonary collapse. For purposes of comparison, we must now consider total unilateral pneumonia and total unilateral pleural effusion, from the same standpoint.

When pneumonia involves an entire lung, the spatial relationships are not changed significantly. The normal clear space of the anterior mediastinum in the lateral view is neither increased nor decreased in size. Even though the anterior portion of one lung is consolidated, the corresponding part of the opposite

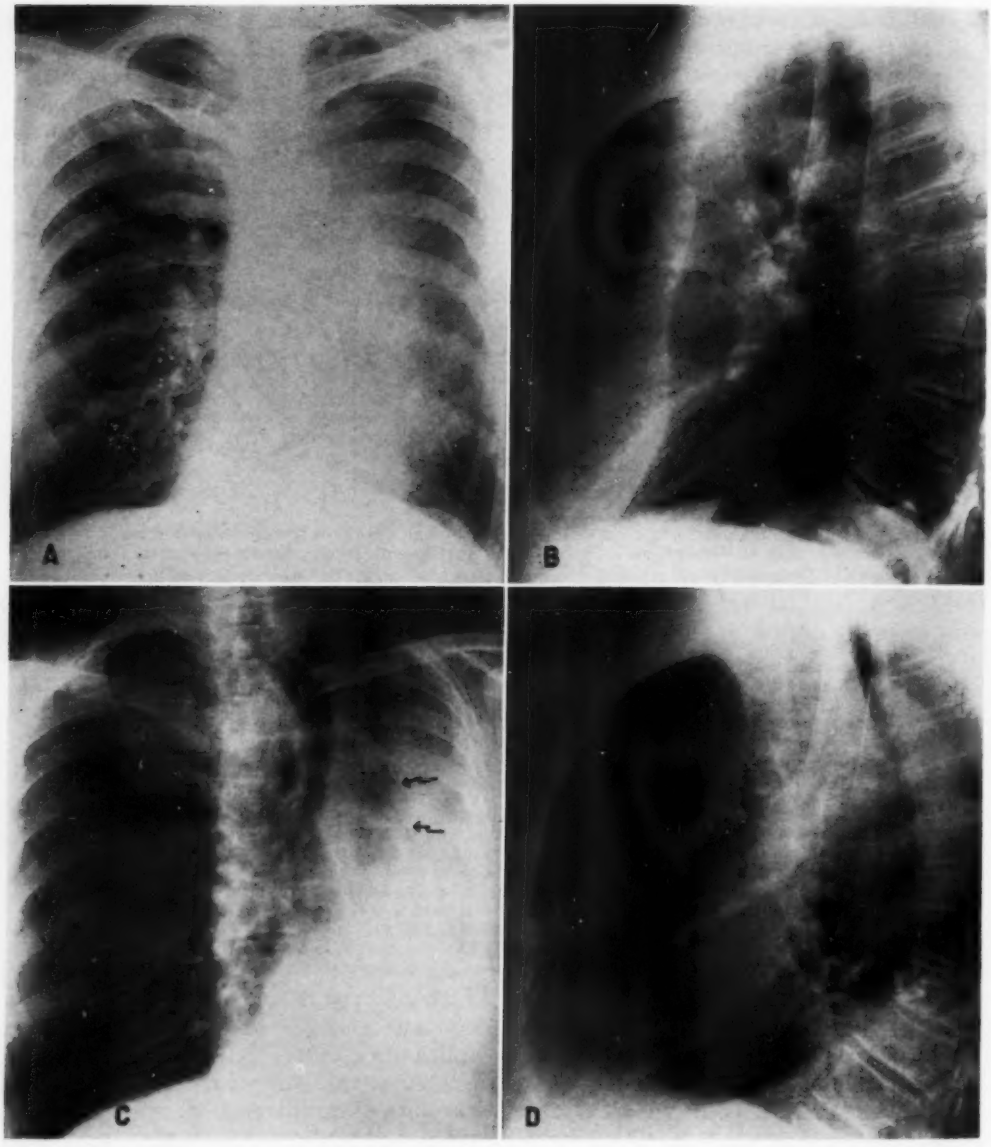

Fig. 3. Left upper lobe collapse (carcinoma) continuing to total unilateral pulmonary collapse.

A. Postero-anterior view illustrating left upper lobe collapse.

B. Lateral view corresponding to A. Interlobar fissure shifted anteriorly with increased density of the collapsed lobe. Retrosternal space enlarged and more radiolucent, due to hyperaerated right lung.

C. Postero-anterior film in total unilateral collapse. Herniation of right lung (arrows) is greater than the degree of shift of the trachea, illustrating the differential mobility of the mediastinum.

D. Lateral view corresponding to C. Considerable increase in size and radiolucence of retrosternal space. Heart and ascending aorta pushed posteriorly. Interlobar fissure no longer seen because both lobes are collapsed and of equal density. Posterior border of heart and left leaf of diaphragm lost against collapsed, airless left lung. A portion of the herniated right lung behind the heart is in contact with the collapsed left lung (arrow), creating a silhouette effect. This posterior herniation also outlines the arch and descending portions of the aorta. See also Figs. 5, C and 9, D.

A and B used in previous report on lobar collapse (2).

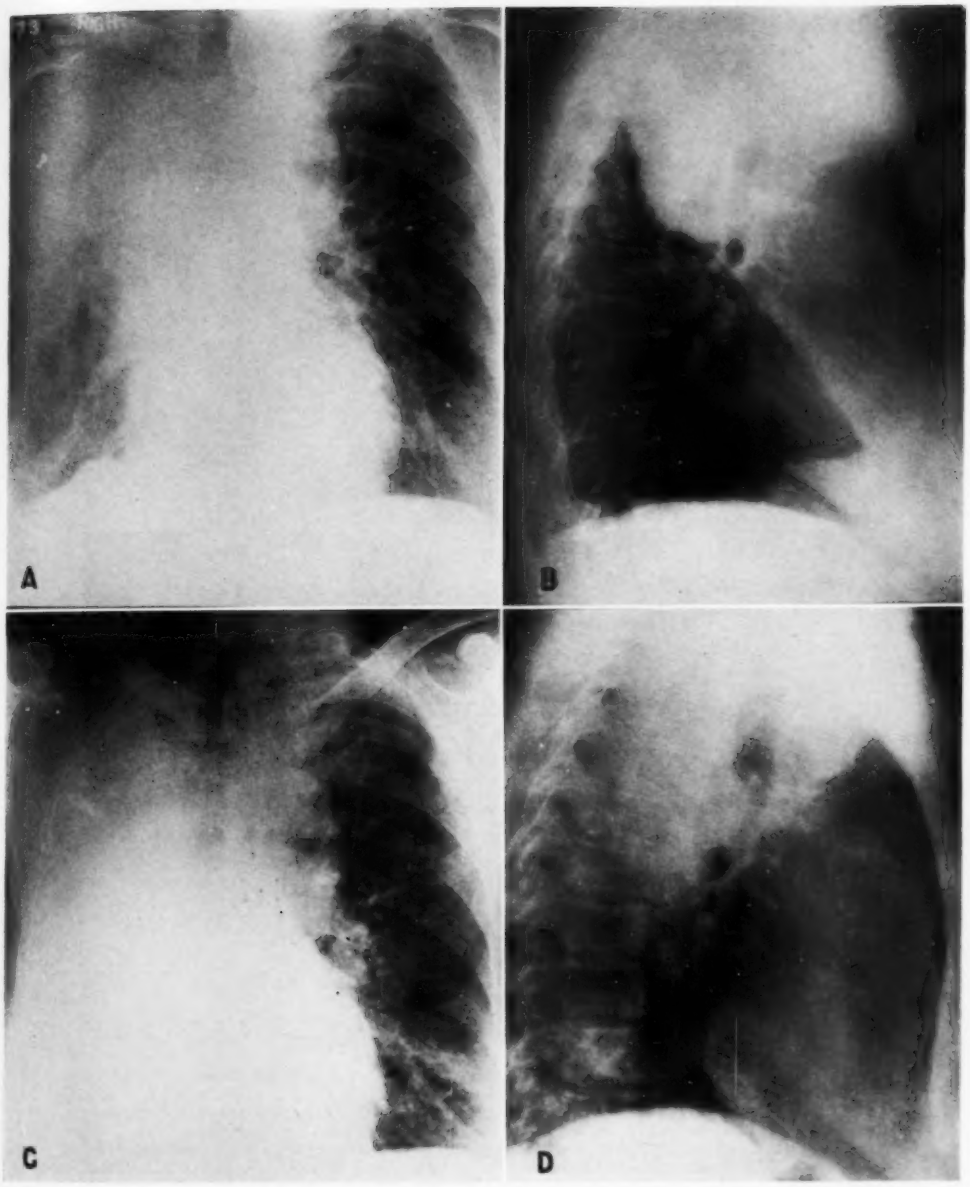

Fig. 4. Right upper and middle lobe collapse due to mucous plugs in an aged patient who had large bronchial adenoma in the right upper lobe. Later, total lung collapse occurred. Each time collapse was relieved by bronchoscopic aspiration.

A. Postero-anterior film in upper and middle lobe collapse.

B. Lateral view corresponding to A, showing slightly prominent retrosternal space. The anterior cardiac border is sharply outlined by over-expanded left lung. The bulge in the upper part of the long fissure is due to a large bronchial adenoma.

C. Postero-anterior film in total collapse of right lung, at later date.

D. Lateral film of totally collapsed right lung. The shadow of the adenoma and right leaf of the diaphragm are lost because of contact with adjacent airless lung. Similarly, the interlobar fissure has disappeared. The anterior mediastinum is more radiolucent than usual, but partially overlapped by the arm shadow. The posterior cardiac margin is seen because it is in contact with aerated left lung. The axillary margins of the scapulae and poorly defined tumor mass obscure the arch and upper descending aorta (insufficient penetration). Detail in the left lung well shown.

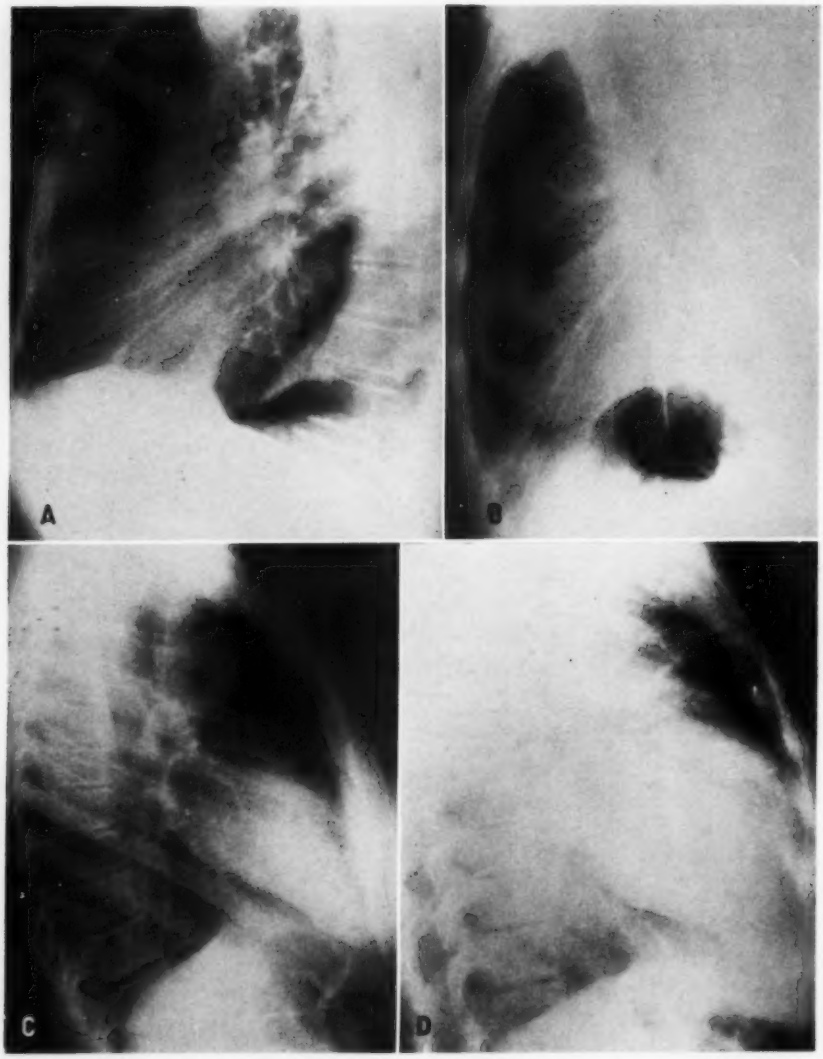

Fig. 5. Four different cases of unilateral pulmonary collapse due to neoplasm. Two right; two left.

A. Although the neoplasm was originally in the left lower lobe, the appearance is practically the same as in 3, D and 9, D. (This figure courtesy of Dr. John D. Osmond, Jr.)

B. Neoplasm originally in left lower lobe. The postero-anterior view showed some shift to the left. The degree of collapse and posterior shift of lung are not as great as in A. Posteriorly some detail is lost because of under-penetration, but the basic appearance is similar.

C. Neoplasm originally in right middle lobe. A postero-anterior view showed a totally opaque right side with slight shift of the mediastinum to the right. At first glance this looks like a normal lateral view, but there is some increase in size and radiolucence of the retrosternal space and the right diaphragmatic shadow is absent. The ascending aorta is lost within the shadow of the airless right lung. Detail in the left lung is well seen. ("Uniform filter effect" with adequate roentgen penetration.)

D. Neoplasm on the right side (site of origin within the lung not determined). A postero-anterior view showed complete density but very little mediastinal shift. There is some increase in radiolucence but no increase in the size of the retrosternal space, indicating minimal rotational effect. The posterior border of the heart is well seen, because it is in contact with aerated left lung; the ascending aorta is not seen because it is in contact with airless right lung.

Where there is marked collapse, as in A, rotational effects predominate (Figs. 1, B and 2, C). Where the amount of collapse is less, as in B, C, and D, due perhaps to tumor bulk and/or associated inflammation, there is much less rotation (Fig. 2, B); the "uniform filter effect" predominates.

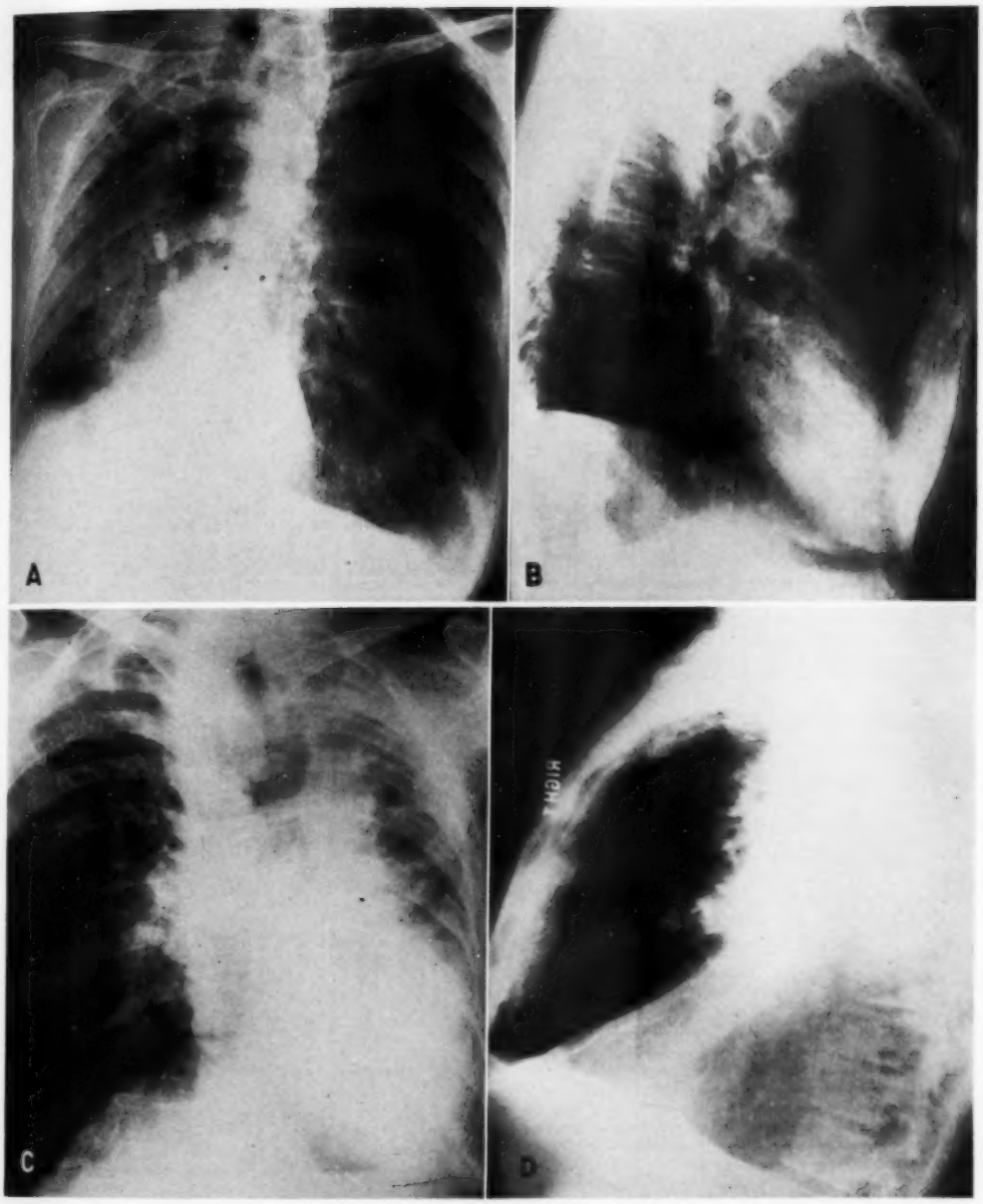

Fig. 6. Two cases of collapse not due primarily to endobronchial block (chronic infection and fibrosis).
A. Postero-anterior view. Right lung shrunken but fairly well aerated. Contraction of right hemithorax.
B. Lateral view corresponding to A. Marked retrosternal and retrocardiac clear space. The posterior border of the heart is visible. Both leaves of the diaphragm are seen because the collapsed right lung is not airless, although there is some pleuritis.
C. Postero-anterior view of another case. Left lung shrunken with only spotty aeration; probably pleuritis with parenchymal fibrosis and consolidation.
D. Lateral view corresponding to C. Marked retrosternal clear space. The heart is displaced posteriorly to a marked degree. The retrocardiac space is therefore diminished and is lost in the density of the left lung and pleura, which also conceals the posterior heart border and left leaf of the diaphragm.

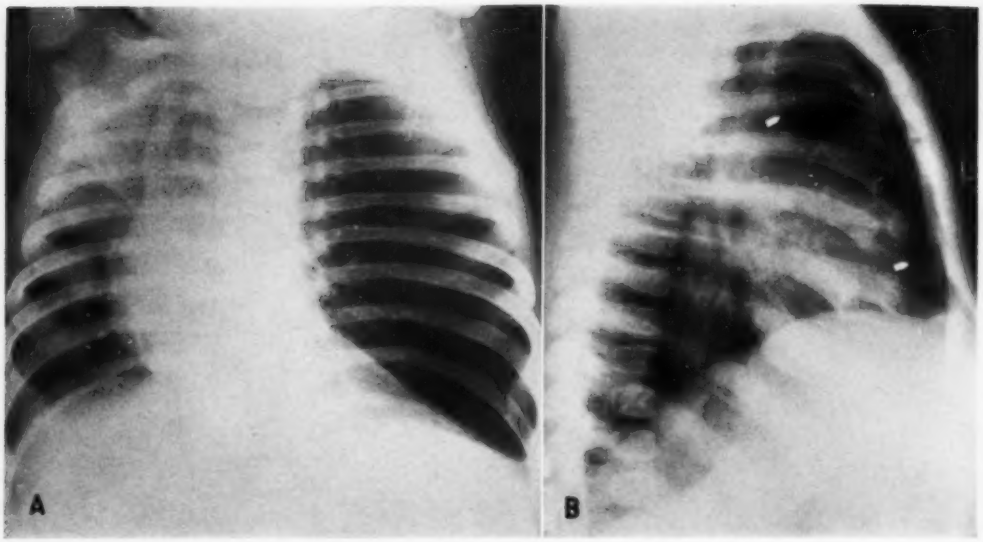

Fig. 7. Lobar emphysema, left upper lobe.
A. Postero-anterior view showing displacement of the mediastinum to the right by the distended left upper lobe.
B. In the lateral view the retrosternal space is increased. Arrows point to the anterior margin of the heart and ascending aorta outlined against the herniated left lung. The right leaf of the diaphragm is seen because the right lung is aerated.
Courtesy of Dr. Daniel Keating.

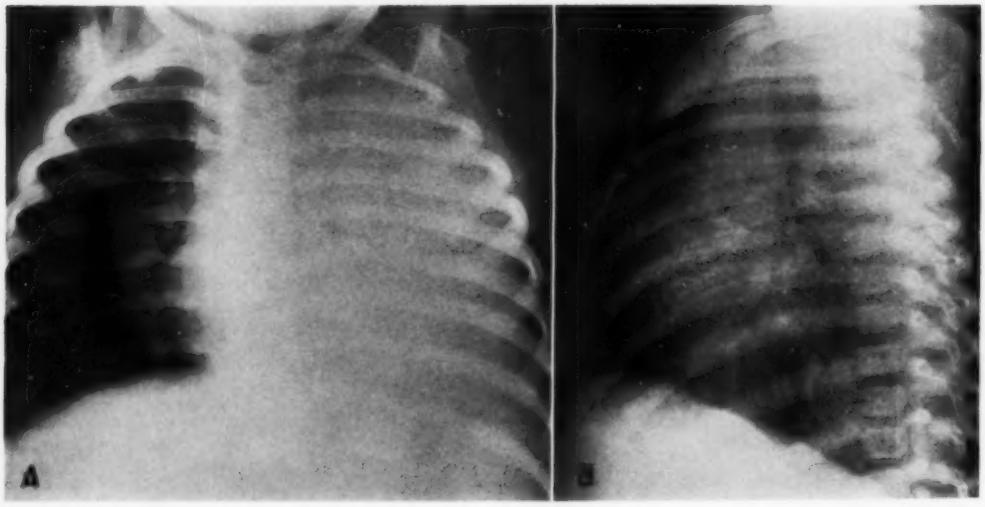

Fig. 8. Total pneumonia on left.
A. Postero-anterior view. Consolidation without shift of the mediastinum.
B. Lateral view shows normal retrosternal space. The posterior border of the heart, left leaf of the diaphragm, and retrocardiac space are obliterated because they are in contact with consolidated lung. A "uniform filter effect" is present because the lung is airless but not displaced.

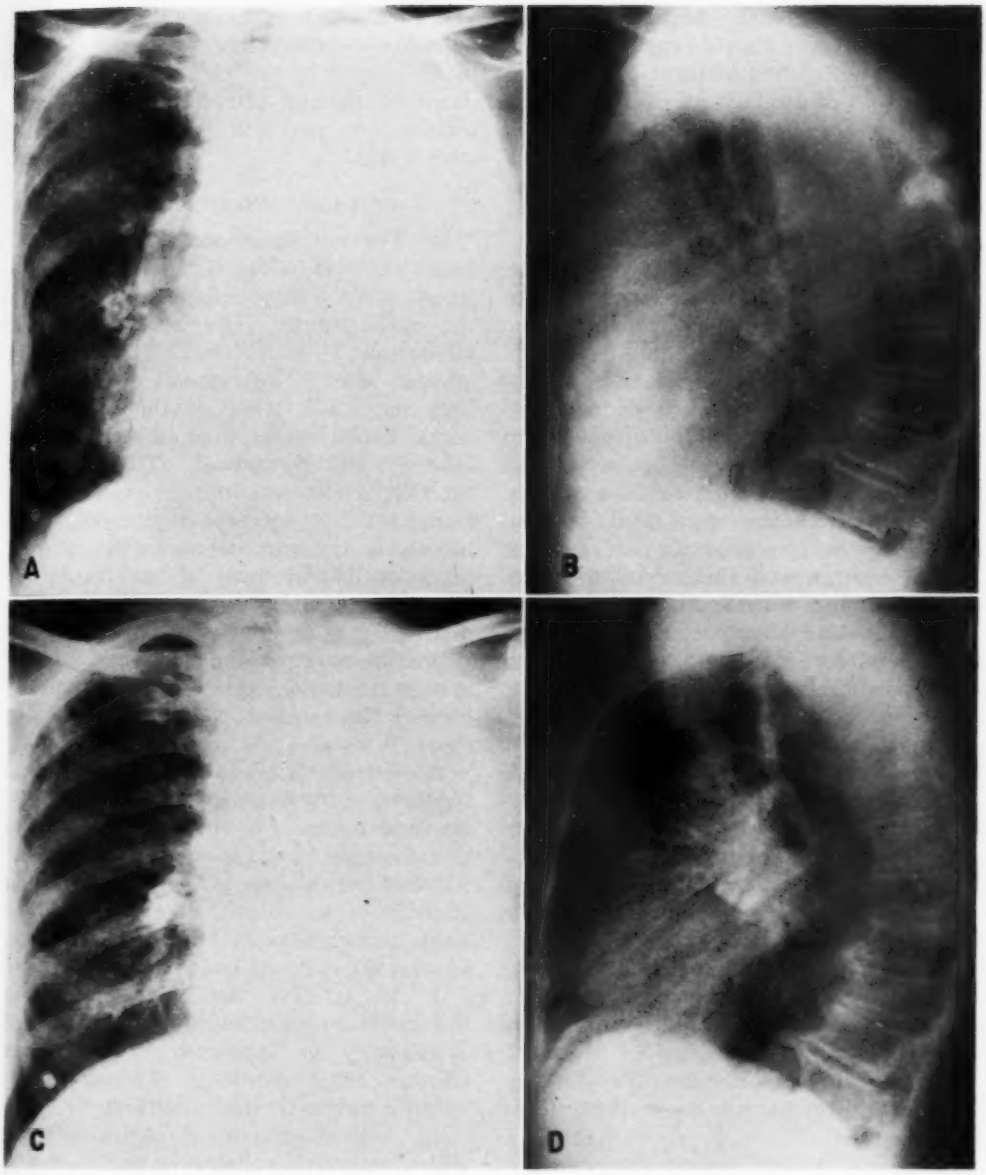

Fig. 9. Combination of collapse (due to endobronchial neoplasm) and fluid (due to pleural metastasis).
A. Postero-anterior view. Left hemithorax opaque. Heart displaced to right.
B. Lateral view corresponding to A. The retrosternal and retrocardiac spaces are hazy. Some detail in the right lung can be seen. The posterior border of the heart is faintly seen, because the laterally displaced atrium protrudes for a greater distance into the right lung. Massive fluid overshadows collapse.
C. Postero-anterior view after removal of pleural effusion. The left hemithorax is still opaque but the heart and mediastinum are now displaced to the left.
D. Lateral view corresponding to C. The appearance of total collapse is the same as in 3, D and 5, A. Arrow points to edge of collapsed left lung in contact with herniated right lung.

lung is aerated and contributes radiolucency to the lateral roentgenogram. The effect of the consolidation in the lateral view is that of a relatively evenly applied filter; if the roentgen penetration is adequate, the anterior mediastinum is still seen as a shadow of diminished density. The factors which govern visualization of the posterior heart border and the descending aorta are generally the same as those discussed under collapse. There will, of course, be no displacement of these structures or of the normal lung.

In the presence of a massive pleural effusion, the mediastinum is displaced to the opposite side. The fluid displaces the homolateral lung from the space in front of the heart; the bulging anterior mediastinum displaces the opposite lung also. The fluid, in contact with the anterior cardiac margin and the ascending aorta, obliterates the normal difference in density (silhouette effect). The appearance in the lateral view is thus one of an overall homogeneous grayness, the fluid acting as a filter of approximately even density. Once again, the ability to distinguish the posterior cardiac border and the descending aorta depends on whether these structures are surrounded by fluid, or whether they remain partly in contact with the opposite, aerated lung. The homolateral diaphragm, as in pneumonia or airless collapse, is obliterated.

The effect of total effusion on the appearance of the anterior mediastinum in the lateral roentgenogram is the converse of the appearance in collapse. However, if the effusion is not massive, there may be no effect on the appearance of the anterior mediastinum.

Combinations of pneumonia, collapse, and fluid may occur. When collapse and pneumonia occur together, the appearance in the lateral view is that of collapse. A very large pleural effusion, however, will overshadow either pneumonia or collapse when they are also present (Fig. 9). Obviously the appearance in the postero-anterior film is of great importance in the differential diagnosis.

It should be remembered that in chronic pulmonary emphysema, with an increase in the depth of the thorax, the anterior mediastinum and retrocardiac spaces are usually large and quite radiolucent in the lateral view.

SUMMARY AND CONCLUSIONS

1. The net difference in pressure between the two halves of the thorax which results when a lung collapses is exerted on the mediastinum. The weaker, anterior mediastinum shifts most toward the affected side. The normal, contralateral lung moves in front of the heart and aorta, displacing the affected lung postero-laterally and downward. This accounts for the appearance in the lateral roentgenogram: (*a*) increase in size and radiolucence of the anterior mediastinum with posterior displacement of the heart and great vessels; (*b*) generalized increase in density postero-inferiorly; (*c*) delineation of the margin of the collapsed lung if it is in contact with opposite, over-expanded lung at the retrocardiac space (silhouette sign).

2. The final appearance in the lateral roentgenogram is independent of the side involved or the site of the original endobronchial block. It is essentially the same whether the collapse is due to constricting pleuritis or to fibrosis, or even when the basic abnormality is obstructive emphysema of the opposite lung.

3. In massive unilateral pneumonia the anterior mediastinum does not change appreciably in appearance; in massive effusion the radiolucent shadow of the anterior mediastinum is obliterated.

4. A large amount of pleural effusion will overshadow collapse or pneumonia in the lateral view.

5. Visualization of the individual structures of the mediastinum will depend on whether they are entirely in contact with fluid, pneumonia, or collapsed airless lung. If there is appreciable contact with the aerated lung in a plane tangential to the ray in the lateral view, they can be distinguished (silhouette effect).

NOTE: We wish to express appreciation to our Associate, Dr. Albert R. Bennett, for the diagrams and to Mr. William Stevenson and Mr. Robert Newhouse of the Department of Photography of Mount Sinai Hospital for the reproductions.

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REFERENCES

1. FELSON, B., AND FELSON, H.: Localization of Intrathoracic Lesions by Means of the Postero-anterior Roentgenogram: The Silhouette Sign. Radiology **55**: 363–374, September 1950.
2. LUBERT, M., AND KRAUSE, G. R.: Patterns of Lobar Collapse as Observed Radiographically. Radiology **56**: 165–182, February 1951.
3. KNUTSSON, F.: The Mediastinal Pleura. Acta radiol. **43**: 265–275, April 1955.

SUMARIO

Colapso Pulmonar Unilateral Total: Estudio del Aspecto Roentgenológico en la Vista Lateral

La diferencia neta en la presión entre las dos mitades del tórax que sobreviene cuando se aplasta un pulmón recae sobre el mediastino. El mediastino anterior, más débil, se desvía más hacia el lado afectado. El pulmón contralateral, normal, se mueve al frente del corazón y de la aorta, desplazando el pulmón afectado posterolateralmente y hacia abajo. Esto explica el aspecto observado en la radiografía lateral: (*a*) aumento del tamaño y de la radiolucencia del mediastino anterior con desplazamiento hacia atrás del corazón y de los grandes vasos; (*b*) aumento generalizado de la densidad posteroinferiormente; (*c*) demarcación más clara del borde del pulmón aplastado si se halla en contacto con el hiperexpandido pulmón opuesto en el espacio retrocardíaco (el llamado signo de la silueta).

El aspecto final en la radiografía lateral es independiente del lado afectado o del sitio del primitivo bloqueo endobronquial. Es en el fondo idéntico ya se deba el colapso a pleuritis constrictiva o a fibrosis, y aun cuando la anomalía fundamental es enfisema oclusivo del pulmón opuesto.

En la neumonía unilateral masiva, el mediastino anterior no varía mayor cosa de aspecto; en el derrame masivo se oblitera la sombra radioluciente del mediastino anterior. Una gran cantidad de derrame pleural eclipsará el colapso o la neumonía en la radiografía lateral.

La visualización de los distintos órganos del mediastino dependerá de si se encuentran totalmente en contacto con líquido, neumonía o pulmón aplastado sin aire. Si existe contacto apreciable con el pulmón aireado en un plano tangencial a los rayos en la radiografía lateral, pueden distinguirse (efecto de silueta).

Evaluation of the Recumbent Esophagogram in the Early Detection of Left Atrial Enlargement[1]

S. SCHORR, M.D., F. DREYFUSS, M.D., and M. FRÄNKEL, M.D.

THE USE OF THE recumbent esophagogram as a means of early detection of an enlarged left atrium has been reported previously (4, 8). It was assumed that such a view might afford an early—possibly the earliest—sign of left atrial enlargement.

Demonstration of a straight esophagus with the patient erect is considered by many clinicians to exclude a diagnosis of mitral valvular disease. It has been our experience, however, that in mild cases the esophagus may appear straight (negative) in the upright position but may show some deviation (positive) on the recumbent esophagogram. On the other hand, we are well aware that such a finding may lead to over-reading of roentgenograms, with diagnosis of mitral valvular disease where none is present. Consequently errors in interpretation may occur in both directions (5).

In the present study we shall report further experiences with this procedure and evaluate its reliability in a larger series of cases.

METHOD

Fluoroscopy of the chest was performed, and postero-anterior teleroentgenograms and left and right anterior oblique films were obtained. The erect esophagogram was taken most often in the right lateral projection, and part of the same film was used for the right lateral recumbent esophagogram. The right lateral view was preferred to the right anterior oblique, since comparison of films is difficult when the angle of obliquity varies even slightly.

All esophagograms were obtained under fluoroscopic control, after most of the barium-swallow had passed down the esophagus. The roentgenograms were taken in mid-inspiration, but fluoroscopy was performed both in deep inspiration and expiration. Fluoroscopy in expiration was done to rule out the possibility that changes in the height of the diaphragm in the recumbent position might cause a localized, well defined imprint in the lower third of the esophagus.

The presumptive clinical diagnosis was formulated in all cases before the x-ray examination.

MATERIAL AND RESULTS

This study is based on 311 cases in which complete clinical and roentgenological data were available, including 173 cases with definite clinical evidence of mitral valvular disease, 17 with probable mitral valvular disease, 7 with various types of congenital heart disease, and a control group of 114 patients without clinical evidence of heart disease of any kind. Among the controls were patients with a high right diaphragm due to various causes, such as pregnancy, kyphoscoliosis, amebiasis of the liver, and phrenic crush. In 105 of this group the erect as well as the recumbent esophagogram showed a straight esophagus, with no localized, well defined indentation. In 18 of these cases a straightening of the left border of the heart, in 2 cases a prominent pulmonary segment, and in 3 straightening of the left heart border together with a prominent pulmonary segment were demonstrable on the postero-anterior and right oblique views (Figs. 1 and 2).

In 3 patients with clinically normal hearts the esophagogram was positive in both the erect and the recumbent view, while no other corroborative x-ray signs of mitral valvular disease were detected. In 6 clinically normal cases only the re-

[1] From the Diagnostic X-ray and Medical Department "A" of the Hadassah University Hospital and Hebrew University Hadassah Medical School, Jerusalem, Israel. Accepted for publication in July 1955.

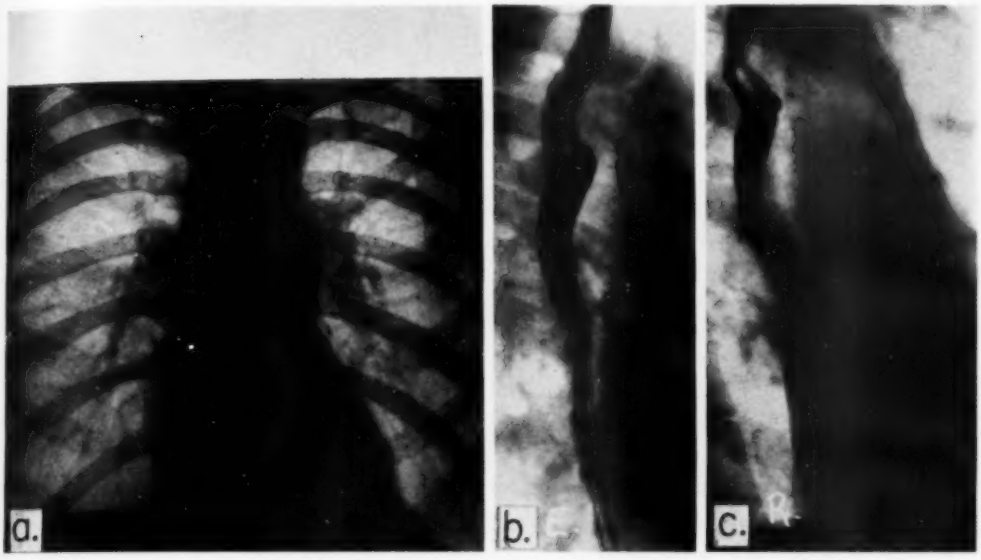

Fig. 1. B.B., female, 46 years old. Clinically normal heart.
a. Postero-anterior view: Heart of normal size and shape. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, negative.

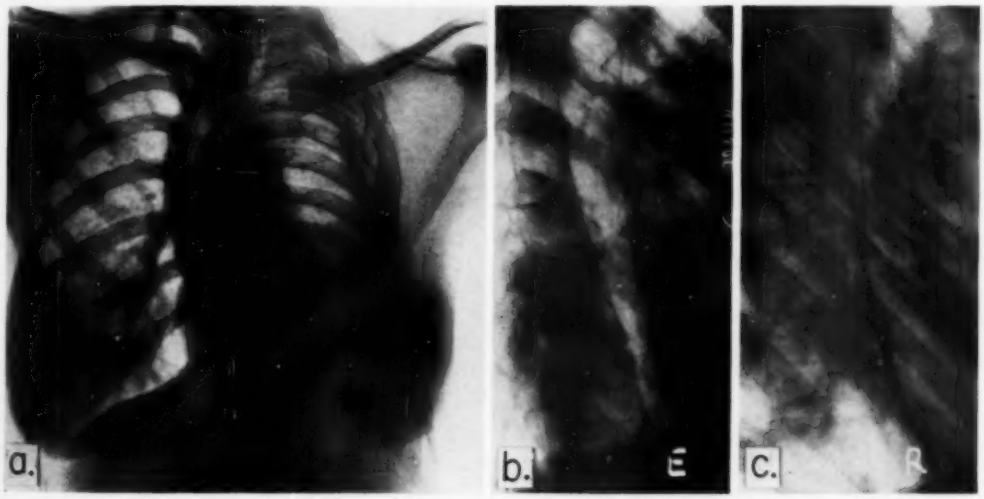

Fig. 2. S.J., female, 35 years old. Clinically normal heart.
a. Postero-anterior view: High left diaphragm. Severe kyphoscoliosis. Normal heart. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, negative.

cumbent esophagogram was positive, while the erect was negative. In 3 of these cases corroborative x-ray signs of mitral disease were obtained (Fig. 3). No case of a clinically normal heart was encountered in which the erect esophagogram was positive and the recumbent negative.

It was not considered of value for the purpose of this study to make any distinction between pure mitral stenosis and mitral insufficiency, occurring either singly or in combination.

There were 62 cases with definite clinical evidence of mitral valvular disease

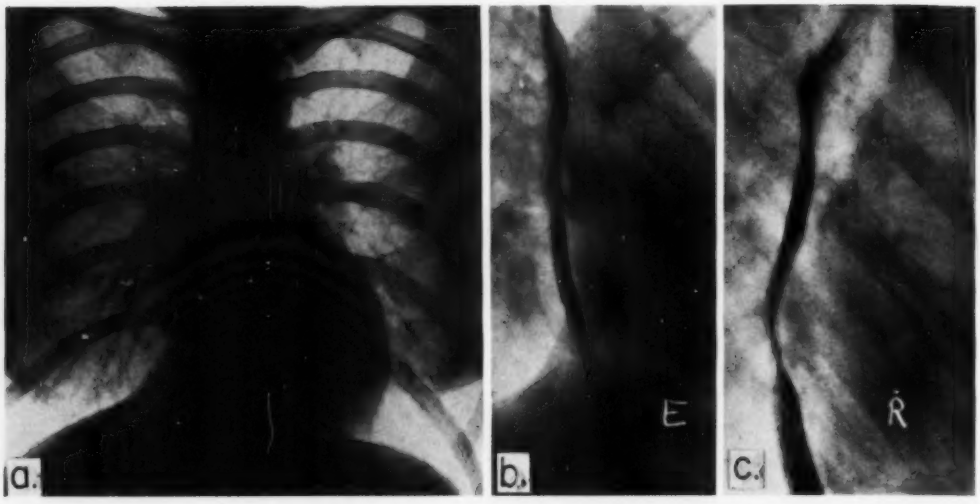

Fig. 3. B.L., female, 20 years old. Clinically normal heart.
a. Postero-anterior view: Heart of normal size and shape. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, positive; minor displacement (false positive?).

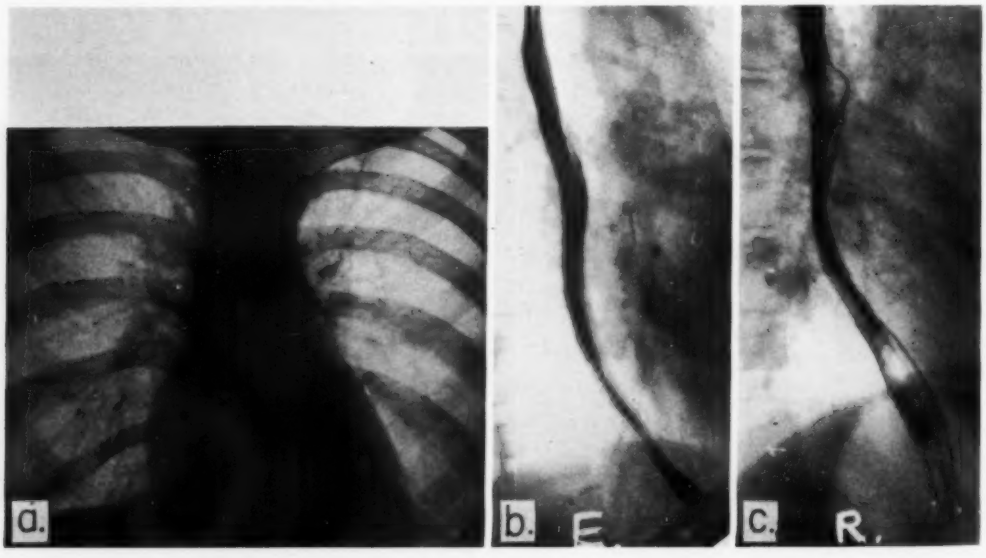

Fig. 4. H.T., female, 23 years old. Clinical diagnosis of mitral valvular disease.
a. Postero-anterior view: Heart of normal size and shape. b. Esophagogram, erect, showing slight posterior displacement. c. Esophagogram, recumbent, showing much deeper and better defined local indentation of the esophagus posteriorly.

and both a positive erect and recumbent esophagogram. Straightening of the left border of the heart was found in 30 cases of this group, prominence of the pulmonary segment in 8, and the two together in 14 cases. The remaining 10 cases showed no x-ray features of mitral valvular disease whatever, except for positive erect and recumbent esophagograms. Although a well localized indentation of the barium-filled esophagus was found in the erect position in the above cases, this

TABLE I: SUMMARY OF CASES

Clinical Diagnosis	Esophagogram		Total No. of Cases	Corroborative X-ray Signs				With No Corroborative X-ray Signs (Cases)
	Erect	Recumbent		PA View: Straightening of the Left Heart Border (Cases)	RAO View: Pulmonary Segment Prominent (Cases)	Straightening of Left Border and Pulmonary Segment Prominent (Cases)	Percentage of Cases With Corroborative X-ray Signs	
Definite mitral valvular disease	+	+	62	30	8	14	84%	10
	—	—	27	7	0	0	26%	20
	—	+	84	31	2	15	57%	36
	+	—	0	0	0	0	..	0
Suspected mitral valvular disease	+	+	5	2	1	0	..	2
	—	—	9	5	0	0	..	4
	—	+	3	1	0	0	..	2
	+	—	0	0	0	0	..	0
Normal heart	+	+	3	0	0	0	..	3
	—	—	105	18	2	3	22%	82
	—	+	6	2	0	1	..	3
	+	—	0	0	0	0	..	0
TOTAL CASES			304					

Note: The 7 patients with congenital heart disease are not included in this table.

was deeper and more clearly defined in the recumbent esophagogram, and the displacement of the mucosal folds from their normally straight course was demonstrated more strikingly in this latter view (Fig. 4).

On the other hand, in a group of 27 patients with mitral valvular disease diagnosed clinically, both the erect and the recumbent esophagogram were found to be negative. In this group the postero-anterior view showed straightening of the left heart border in 7 cases only, while bulging of the pulmonary segment or other x-ray features of mitral disease such as "double contour" were not encountered in any instance.

The group deserving special emphasis consisted of 84 cases of mitral valvular disease diagnosed clinically in which the recumbent esophagogram was positive while the erect esophagogram was negative. Straightening of the left border of the heart was present in 31 of these cases, bulging of the pulmonary segment occurred in 2, while both phenomena were demonstrable in 15. Other x-ray features, such as "double contour" or elevation of the left main bronchus, were not found. In 36 of the 84 cases (43 per cent), no corroborative x-ray signs of mitral valvular disease could be detected apart from the well defined, localized indentation of the barium-filled esophagus in the recumbent position (Figs. 5 and 6).

In this group of 84 patients were 12 children between the ages of four and twelve years and 30 adolescents between thirteen and eighteen years.

It is again to be stressed that in no case with a positive esophagogram in the erect position was a negative esophagogram obtained in the recumbent position.

In the group of 17 cases in which mitral valvular disease was suspected on clinical grounds, the esophagogram in both positions was positive in 5 cases, and corroborative x-ray signs of mitral valvular disease were found in 3. In 9 cases the esophagogram was negative in both positions, though 5 of these showed straightening of the left border of the heart in the postero-anterior view only. In 3 cases only the recumbent esophagogram was positive, and in only 1 was straightening of the left border of the heart noted in the postero-anterior view.

In a small group of children we were able to follow clinically and roentgenologically the course of rheumatic heart disease. At the beginning, no heart murmurs were heard, and the only positive x-ray finding was furnished by the recumbent esophagogram. On re-examination several weeks or months later, heart murmurs consistent with mitral valvular disease were audible,

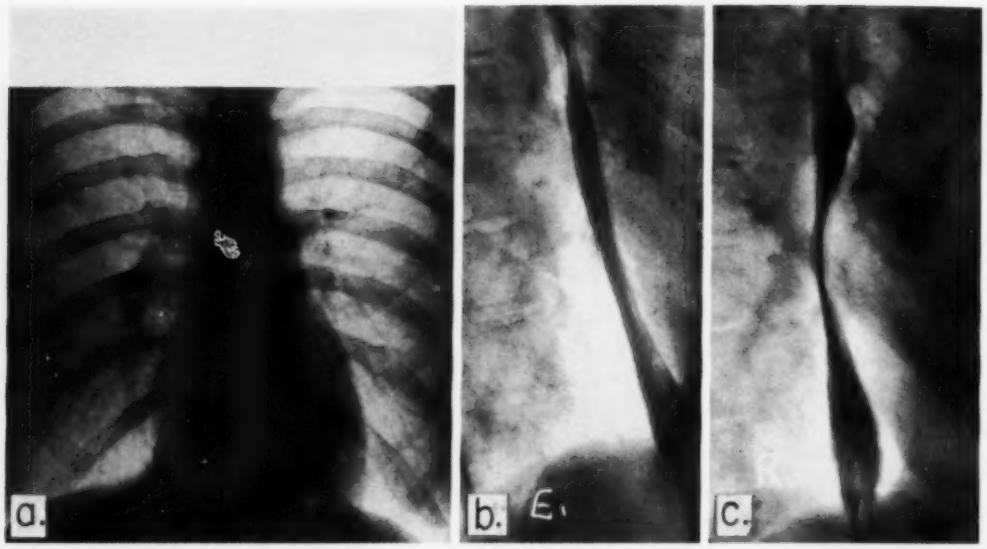

Fig. 5. S.S., female, 19 years old. Clinical diagnosis of mitral valvular disease.
a. Postero-anterior view: Heart of normal size and shape. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, positive. Definite posterior displacement.

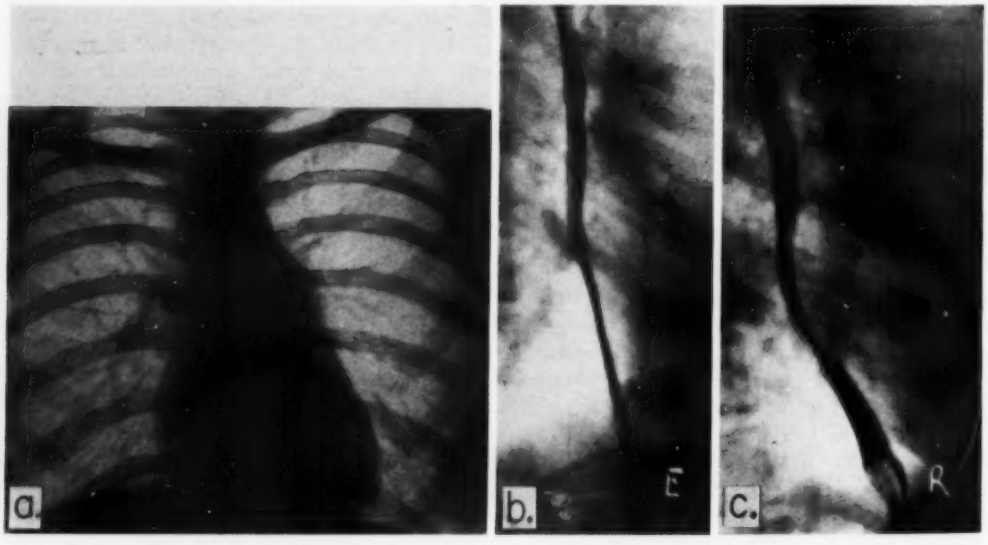

Fig. 6. K.A., female, 19 years old. Clinical diagnosis of mitral valvular disease.
a. Postero-anterior view: Pulmonary segment of left border prominent. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, positive. Definite posterior displacement.

and even the erect esophagogram was positive (Fig. 7).

In other cases the clinical findings consistent with mitral valvular disease were well established, whereas the x-ray signs, including the esophagogram in the recumbent position, were negative. On reexamination, several months later, all x-ray features pointing to mitral valvular disease still remained negative, but the

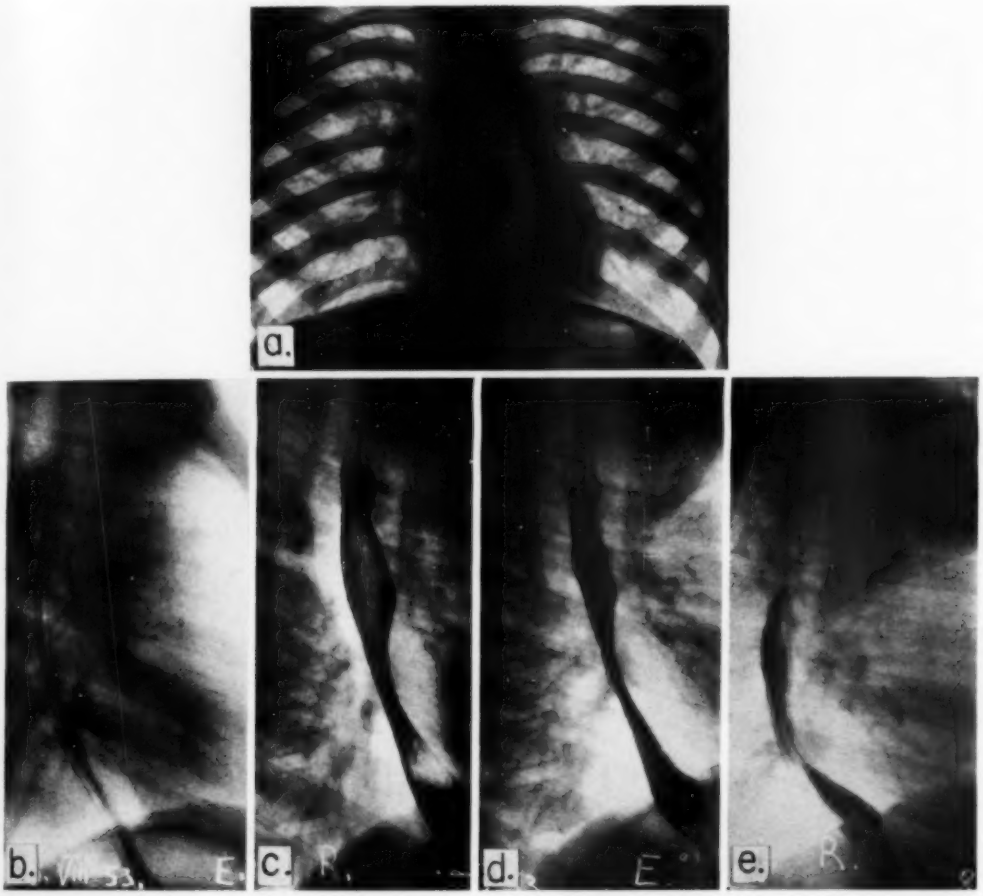

Fig. 7. J.J., male, 11 years old. Rheumatic history, joint swelling and pain, clinically no murmurs audible. First examination Aug. 16, 1953: a. Postero-anterior view, showing slight mitral configuration. b. Esophagogram, erect, negative. c. Esophagogram, recumbent positive. Posterior displacement.
Second examination Sept. 8, 1953. Systolic mitral murmur now audible (confirmed by phonocardiogram). d. Esophagogram, erect, positive, showing posterior displacement. e. Esophagogram, recumbent, showing more marked posterior displacement.

recumbent esophagogram was positive (Fig. 8).

In 7 cases of various types of congenital heart disease, the esophagus followed a straight course both in the erect and in the recumbent position (Fig. 9).

DISCUSSION

According to the nomenclature and criteria for diagnosis of diseases of the heart, the demonstration of left atrial enlargement by radiological means is one of the necessary criteria for a diagnosis of mitral valvular disease. Rigler (7), in 1929, described atrial dilatation as an early and positive sign of disease of the mitral valve and stated that absence of this sign made such a diagnosis doubtful. In not every case of mitral valvular disease, however, is the left atrium enlarged (Epstein, 1; Schwedel, 9; Pariser *et al.*, 6). The reasons for these exceptions are not clear. Kaye *et al.* (3) found backward displacement of the esophagus to be the most frequent positive x-ray feature of mitral valvular disease (75 per cent) but at the same time it was the most frequent "false positive" finding in a con-

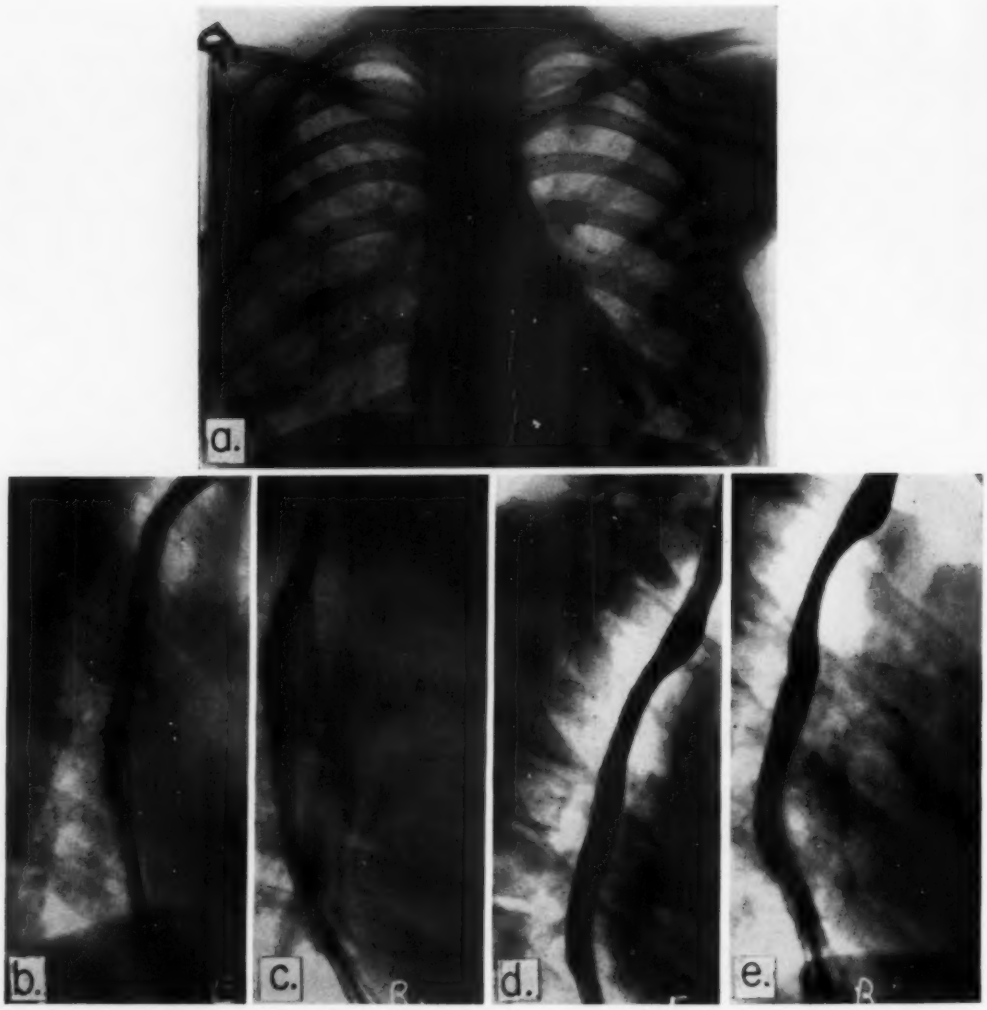

Fig. 8. S.Z., female, 12 years old, with mitral valvular disease diagnosed clinically; also subacute bacterial endocarditis.

First examination Dec. 27, 1951: a. Postero-anterior view, showing heart normal in size and shape. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, negative.

Second examination Aug. 13, 1952: Postero-anterior view unchanged. d. Esophagogram, erect, showing very slight posterior indentation. e. Esophagogram, recumbent, showing definite posterior displacement.

trol group with normal hearts (10 per cent). The incidence of apparently false positives even with the more sensitive procedure of recumbent esophagography in our series of cases is similar (8 per cent).

It is possible that some or all of these cases may represent instances of very early "subclinical" left atrial enlargement; only long term clinical and x-ray follow-up studies can confirm this possibility. In 3 of our 9 cases in which only the recumbent esophagogram was positive there were other corroborative x-ray signs of left atrial enlargement. On the other hand, it is possible that this finding may also be due to minor anatomical variations of no pathological significance.

A high right diaphragm is considered by many as a cause of posterior displacement of the esophagus (Schwedel, Roesler,

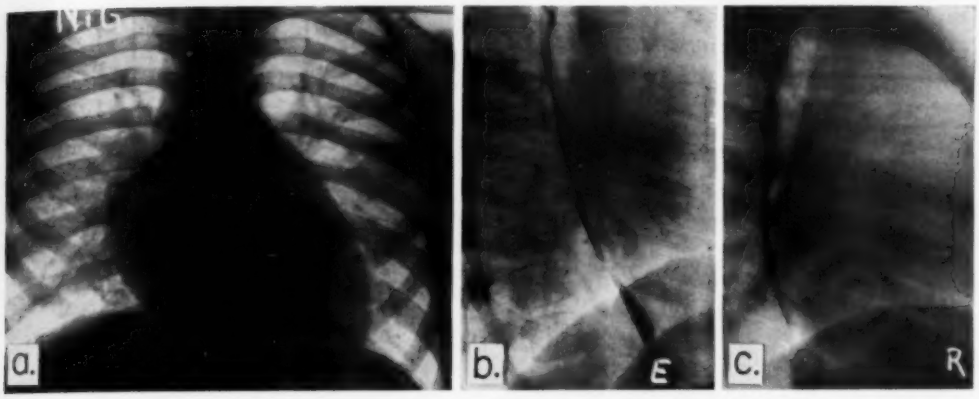

Fig. 9. N.G., female, 5 years old. Congenital heart disease diagnosed clinically (probable interatrial septal defect).

a. Postero-anterior view, showing prominent pulmonary segment of left border. Right heart enlarged. b. Esophagogram, erect, negative. c. Esophagogram, recumbent, negative.

Pillmore, Kaye *et al.*). Displacement due to this cause, however, involves the whole length of the esophagus and is quite different from the well localized retrodisplacement produced in the lower third of the esophagus by an enlarged left atrium. Such retrodisplacement is confined to the area between the bifurcation of the bronchus and a point slightly above the dome of the right diaphragm. This localized displacement of the esophagus was not observed in our series of cases with high right diaphragms and normal hearts.

It is significant that in our series of cases a negative recumbent esophagogram, was never obtained in the presence of a positive erect one.

In the early stages of mitral valvular disease the heart in the postero-anterior view may retain its normal size and contour. Since an erect esophagogram may show a straight esophagus and the only positive x-ray sign present may be that obtained by the recumbent esophagogram, this method should be applied in patients with suggestive rheumatic histories and questionable heart murmurs. In the presence of a positive recumbent esophagogram, the diagnosis of a functional murmur becomes improbable and it must be concluded that organic heart disease is present.

SUMMARY

1. The reliability of the recumbent esophagogram as a sensitive means of detecting mild left atrial enlargement was investigated in 304 patients. Of these, 173 had definite clinical evidence of mitral valvular disease, in 17 the presence of mitral valvular disease was suspected, 114 had clinically normal hearts.

2. In the cases of clinically normal hearts, findings on both the erect and the recumbent esophagogram were normal, except in 8 per cent, where a positive esophagogram, erect or recumbent, was obtained.

3. In 62 cases of mitral valvular disease in which the esophagogram in the erect position was positive, the recumbent esophagogram usually demonstrated a clearer, deeper, and better localized retrodeviation.

4. In 84 cases with mitral valvular disease diagnosed on clinical grounds, only the recumbent esophagogram was positive, and in 36 of these cases there were no other corroborative x-ray signs of the condition.

5. In the group of cases in which mitral valvular disease was suspected by the clinician and corroborative x-ray signs were demonstrated, 9 showed negative and 8 showed positive esophagograms.

6. In no case with a positive erect

esophagogram was there a negative recumbent esophagogram.

7. This study confirms our previous opinion that the recumbent esophagogram is a reliable and sensitive indicator of slight left atrial enlargement.

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REFERENCES

1. EPSTEIN, B. S.: Rheumatic Mitral Valve Disease Without Cardiac Enlargement. Radiology **48:** 249–255, March 1947.

2. EVANS, W.: The Course of the Oesophagus in Health, and in Disease of the Heart and Great Vessels. Medical Research Council, Special Report Series, No. 208. London, His Majesty's Stationery Office, 1936.

3. KAYE, J., MEYER, M. J., VAN LINGEN, B., MCGREGOR, M., AND BRAUDO, J. L.: The Radiological Diagnosis of Mitral Valve Disease. Brit. J. Radiol. **26:** 242–251, May 1953.

4. KJELLBERG, S. R.: The Importance of the Prone Position in the Roentgenologic Diagnosis of Slight Mitral Disease. Acta radiol. **31:** 178–181, 1949.

5. NICE, C. M., JR., AND HALL, C. W.: The Relationship of the Left Atrium to the Opacified Esophagus in Upright and Recumbent Positions. Radiology **65:** 61–64, July 1955.

6. PARISER, S., ZUCKNER, J., TAYLOR, H. K., AND MESSINGER, W. J.: Mitral Stenosis Without Clinically Demonstrable Left Auricular Enlargement. Am. J. M. Sc. **221:** 431–439, April 1951.

7. RIGLER, L. G.: The Visualized Esophagus in the Diagnosis of Diseases of the Heart and Aorta. Am. J. Roentgenol. **21:** 563–571, June 1929.

8. SCHORR, S., DREYFUSS, F., AND SCHWARTZ, A.: The Recumbent Esophagogram. An X-Ray Method for Early Detection of Left Atrial Enlargement. Radiology **57:** 208–213, August 1951.

9. SCHWEDEL, J. B.: Clinical Roentgenology of the Heart. Annals of Roentgenology Series, Vol. 18. New York, Paul B. Hoeber, Inc., 1946.

10. SOSMAN, M. C.: Subclinical Mitral Disease. J.A.M.A. **115:** 1061–1066, Sept. 28, 1940.

SUMARIO

Justipreciación del Esofagograma en Decúbito en el Descubrimiento Temprano de la Hipertrofia de la Aurícula Izquierda

En 304 enfermos, se investigó la fidedignidad de los esofagogramas obtenidos en la posición recostada como medio sensible para descubrir la hipertrofia de la aurícula izquierda. De ellos, 173 tenían signos clínicos bien definidos de afección de la válvula mitral, en 17 se sospechaba la existencia de dicha afección y 114 tenían corazones clínicamente normales. En estos últimos enfermos, con pocas excepciones, los hallazgos arrojados por el esofagograma en las posiciones tanto erguida como recostada fueron normales. En 8 por ciento de este grupo, se obtuvo un esofagograma positivo, con el enfermo ya de pie o recostado.

En 62 casos de insuficiencia mitral, en que era positivo el esofagograma en la posición erguida, el tomado en la posición recostada reveló casi siempre una retrodesviación más clara, más intensa y mejor localizada.

En 84 casos con insuficiencia mitral diagnosticada a base clínica solamente, el esofagograma en decúbito resultó positivo, y en 36 de estos casos no había otros signos roentgenológicos corroborativos.

En el grupo de casos en que sospechaba afección de la válvula mitral el clínico y se encontraron signos roentgenológicos corroborativos, 9 revelaron esofagogramas negativos y 8 positivos.

En ningún caso con esofagograma positivo en posición erguida, resultó negativo el esofagograma en decúbito.

Confirma este estudio la opinión abrigada por los AA. desde antes, de que el esofagograma en decúbito es un indicador fidedigno y sensible de la hipertrofia leve de la aurícula izquierda.

Roentgen Manifestations of Milk Drinker's Syndrome[1]

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THE ROENTGEN finding of calcinosis in the presence of a history of prolonged and excessive milk consumption (usually for peptic ulcer) and renal insufficiency should indicate the diagnosis of milk drinker's syndrome. It is our purpose in this paper to present the clinical syndrome, demonstrate its roentgen manifestations, and discuss its pathological physiology.

HISTORICAL

In 1949, Burnett *et al.* (3) described a syndrome following prolonged intake of excessive quantities of milk and alkali. The essential components were hypercalcemia without hypercalcuria or hypophosphatemia, calcinosis manifested by band keratitis, renal insufficiency with azotemia and mild alkalosis, and improvement on a diet low in milk and absorbable alkali. The cases resembled hyperparathyroidism with renal insufficiency but were differentiated from the latter by normal urinary calcium, normal or elevated serum phosphorus, absence of skeletal demineralization, and lowering of serum calcium on a low calcium diet. On theoretical grounds the authors thought that a combination of elevated serum calcium and normal or slightly elevated phosphorus would predispose to metastatic calcinosis. The calcinosis was uniformly present as band keratitis, but in only one instance as widespread subcutaneous calcifications. Elimination of milk from the diet resulted in significant lowering of serum calcium and phosphorus.

ROENTGEN FINDINGS

The characteristic roentgen appearance of metastatic calcinosis is one of calcific deposits in the subcutaneous tissues, usually in proximity to joints. The masses are amorphous; they vary in size from nodules to bulky tumors, and are unaccompanied by change in osseous structure. Ancillary findings include widespread calcifications in blood vessels, falx cerebri, kidneys, and lungs.

PATHOLOGICAL PHYSIOLOGY

Albright (1) stated that in primary hyperparathyroidism elevated serum and urinary calcium predispose to the formation of calcium phosphate and oxalate stones. Later, nephrocalcinosis causes renal failure and phosphorus retention. At this stage, kidney damage is no longer reversible. Secondary hyperparathyroidism following chronic renal disease occurs when phosphorus retention causes a lowering of serum calcium which, in turn, stimulates the parathyroid glands. Rebound elevation of calcium results, and in time metastatic calcinosis occurs.

Wermer *et al.* (7) postulated the role of the kidney to be the same regardless of the parathyroid function. They concluded that the prerequisite for calcinosis is saturation of the circulating blood with calcium and phosphorus. Renal calcinosis occurs when the two cations are precipitated in the postglomerular parenchyma. Later the disease progresses to metastatic calcinosis, occurring in normal tissue in contradistinction to the dystrophic tissues calcified in scleroderma.

Snapper (6) concluded that it is difficult to explain metastatic calcinosis solely by oversaturation of the tissues by calcium phosphate. His theory was that calcium is deposited preferentially in organs where the excretion of acid results in temporary tissue alkalinity, which favors precipitation of calcium carbonate and phosphate. An explanation is thus offered for the fact that the kidneys and lungs, but not the

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Figs. 1 and 2. Case I. Giant amorphous calcific deposits in the soft tissues of the right shoulder (Fig. 1) and in the soft tissues overlying both hips, in the buttocks, and overlying the sacrum (Fig. 2). There is no osseous abnormality.

subcutaneous tissues, are preferred sites of calcinosis.

Kirsner and Palmer (5) found that prolonged alkali therapy of peptic ulcer, complicated or uncomplicated by alkalosis, does not result in permanent impairment of renal function in patients with previously normal kidneys. Becker *et al.* (2) reported a 36 per cent incidence of renal calcinosis in 99 autopsied cases of chronic duodenal ulcer. Their hypothesis was that high calcium intake and transient episodes of alkalosis cause calcinosis. In none of their cases did irreversible renal failure occur.

Dworetzky (4) reported a case of milk drinker's syndrome in a patient with peptic ulcer who had impaired renal function and calcinosis, reversible on a normal diet with aluminum hydroxide. The patient had been on a Sippy regime with excessive milk intake for sixteen years. Despite three years of careful dietary management, renal insufficiency persisted.

COMMENT

We believe that conflicting theories of the pathogenesis of calcinosis in the milk drinker's syndrome can be unified into one concept. The *sine qua non* is prolonged excessive consumption of milk. The blood becomes saturated with calcium and phosphorus, which are precipitated in the renal tubules and parenchyma. If alkalosis is present, the kidneys excrete an increased quantity of acid. As a result, the rate of precipitation of calcium salts in the kidney is increased. Once renal insufficiency supervenes, excretion of calcium tends to be fixed, and the serum levels of both cations remain elevated. Metastatic calcinosis and further nephrocalcinosis result, with perpetuation of the cycle. Elimination of milk from the diet can bring about a return of serum calcium and phosphorus to normal and can reverse metastatic calcinosis but cannot significantly reverse renal insufficiency. When metabolic acidosis develops in the course of uremia, calcinosis progresses so long as milk consumption continues. In the medical management of peptic ulcer, therefore, periodic determinations of serum calcium, nonprotein nitrogen, and CO_2-combining power are advisable. If the findings are abnormal, elimination of milk and absorbable alkali from the treatment regime is indicated.

CASE REPORTS

Two cases are presented in detail to illustrate the evolution of milk drinker's syndrome.

CASE I: F. S., a 55-year-old white male, was transferred to the Psychiatric Division of Bellevue Hospital on Oct. 19, 1954, from another hospital. Incision and drainage of a chronic right subdeltoid bursitis had been done on Oct. 3, with subsequent infection. On admission, the patient was febrile, confused, and emaciated in appearance. There was a draining sinus below a healed scar on the right shoulder. Overlying the right buttock was a firm mass measuring 8 × 10 inches. A similar mass, 4 × 5 inches, overlay the left buttock, and anterior to the right hip was a third mass, 4 inches in diameter.

The patient gave a history of intermittent postprandial epigastric pains of twelve years duration, related to greasy foods and relieved by vomiting or drinking milk. He admitted to drinking 3 to 4 quarts of milk daily for eleven years, with a recent reduction to 1 to 2 quarts and occasional use of bicarbonate of soda. Nine years earlier he first noticed a mass on the left elbow. It was excised but recurred. The next year a similar mass was removed from the left shoulder and diagnosed as chronic calcific bursitis. Six years previously masses appeared over both hips and continued to grow. One year prior to admission, biopsy of a right subdeltoid bursitis was done elsewhere and calcinosis was reported.

According to the Records Division, the patient had been examined in June 1954, at the Bellevue Hospital Employability Clinic. Pertinent physical findings at that time included masses, similar to those described above, over both hips and the right shoulder. Laboratory data revealed a moderate normocytic anemia and renal insufficiency. Roentgen studies disclosed a normal chest, deformed duodenal bulb, and giant calcific deposits in the soft tissues of the right shoulder (Fig. 1) and pelvis, overlying both hips and the sacrum (Fig. 2). A diet low in calcium and fat, with no milk, was prescribed.

Laboratory data on admission were: hemogram: hemoglobin 8.5–11.5 gm. (after transfusions); hematocrit: 26–34 per cent; urinalysis: sp. gr. 1.006–1.010; $CaCO_3CaPO_4$ crystals; blood chemistry: non-protein nitrogen 150 mg. per cent, gradually reduced to 56–80 mg. per cent; creatinine 3.6–1.0 mg.; CO_2-combining power 32, 44, 44 vol. per cent; serum calcium on restricted milk diet 9.4–9.8 mg. per cent, on milk *ad lib.* 12.5–13.6 mg. per cent; serum phosphorus initially 7.2 mg. per cent, low of 3.3 on restricted milk diet, average and mean value 5.6; renal function studies: PSP excretion 5 per cent in fifteen minutes, 15 per cent in forty-five minutes; urea clearance 21 c.c./min.; twenty-four-hour urine calcium output on milk-free diet 34, 41 mg., with milk *ad lib.* 96, 203, 382 mg.

There were dense white plaques in both tympanic membranes, interpreted as calcific deposits, and limbal calcific infiltrates, described as band keratitis.

Roentgenograms of the chest showed calcific deposits in the aortic knob, left axilla, and both cervical regions. A gastrointestinal study revealed a persistently deformed duodenal bulb due to chronic duodenal ulcer. The osseous structure appeared normal. There were extensive calcification in peripheral blood vessels and giant amorphous calcific deposits in the soft tissues overlying both hips and, to a lesser extent, the right shoulder (Fig. 3). Comparison with the film taken in June of 1954 showed the calcific deposit in the right shoulder to be greatly decreased in size.

Fig. 3. Case I. Roentgenogram obtained four months after Fig. 1, showing considerable resorption of the calcific deposits in the right shoulder.

The patient improved clinically, but chronic renal insufficiency persisted. On a low calcium diet, the serum calcium fell to normal and serum phosphorus towards normal. When milk was given without restriction, the findings were reversed.

This was a case of milk drinker's syndrome following prolonged excessive consumption of milk with reversible metastatic calcinosis, elevated serum calcium and phosphorus reversible on a milk free diet, and chronic irreversible renal insufficiency with acidosis. Previously, the condition had been erroneously diagnosed as chronic calcific bursitis.

CASE II[2]: E. B., a 67-year-old white male, was admitted to Bellevue Hospital on Feb. 1, 1949, complaining of postprandial abdominal pain and vomiting of several months duration. Since 1928 he had been treated intermittently for pulmonary tuberculosis. In 1936 a gastrointestinal study done

[2] Previously reported by Wermer *et al.* (7).

Fig. 4. Case II. Amorphous calcific deposits overlying the right clavicle, upper scapula, and head of humerus. The findings are confined to the soft tissues.

because of recurrent abdominal pain revealed a duodenal ulcer. The patient was placed on the Sippy regime, with considerable relief of symptoms. During the following thirteen years he adhered to a dairy diet, taking 2 to 3 quarts of milk daily, supplemented by Sippy powders and alkalis. Eighteen months prior to admission tender swellings developed on the back, right shoulder, and right wrist.

Physical examination revealed rubbery masses 6 to 8 cm. in diameter overlying the inferior angle of the scapulae. Similar irregular masses were present over the right wrist and acromioclavicular joint, without limitation of motion. Band keratitis was present bilaterally.

The sputum was positive for acid-fast bacilli. Blood studies revealed a mild anemia; blood urea nitrogen, 58–61 mg. per cent; serum calcium 10.8–11.8 mg. per cent; serum phosphorus 3–5 mg. per cent; alkaline phosphatase 3–5 Bodansky units; total proteins 7.2 gm., with an albumin-globulin ratio of 4.9/2.3; Co_2-combining power 14–38 vol. per cent. Urinary findings were: specific gravity 1.007–1.010; albuminuria; pyuria; PSP excretion less than 5 per cent; forty-eight-hour calcium output 312 mg.

Roentgen studies revealed bilateral pulmonary tuberculosis, chronic duodenal ulcer, and large irregular amorphous calcific deposits at the inferior margin of the scapulae, over the right acromioclavicular joint (Fig. 4), and over the distal ulna (Fig. 5).

The hospital course was progressively downhill, with control of symptoms by a regular diet plus Sippy powders. Biopsy of the right scapular mass showed calcium granules in an eosinophilic matrix. Transurethral prostatectomy was done to relieve dysuria and frequency. Milk and alkali were removed from the diet, and over a period of months the subcutaneous calcifications underwent resorption. The blood count, blood chemistry, and renal function did not improve. Serum calcium was 9.2–13.1 and phosphorus was 1.9–4.0 mg. per cent. The patient began to vomit persistently, grew weaker, lost weight, and became uremic. Death occurred after thirteen months of hospitalization.

Autopsy findings included chronic duodenal ulcer; metastatic calcifications in the lungs, kidney, and subcutaneous tissues; chronic glomerulonephritis; mild parathyroid hyperplasia; atherosclerosis of the aorta with calcification.

Fig. 5. Case II. Amorphous calcific deposit in the soft tissues overlying the distal end of the right ulna.

This was a case of milk drinker's syndrome following prolonged excessive intake of milk and alkali, with metastatic calcinosis reversible on a milk-free diet, intermittently elevated serum calcium and phosphorus before and after a milk-free diet, and chronic renal insufficiency, acidosis and uremia, causing death.

SUMMARY

1. Two cases of milk drinker's syndrome with metastatic calcinosis and chronic renal insufficiency are presented.

2. Roentgen diagnosis and subsequent management of the disease are described.

3. The altered physiology resulting from the prolonged and excessive consumption of milk is discussed. Reversibility of calcinosis and high serum calcium and phosphorus on a milk-free diet are stressed.

REFERENCES

1. ALBRIGHT, F.: The Parathyroids—Physiology and Therapeutics. J.A.M.A. **117:** 527–533, Aug. 16, 1941.
2. BECKER, D. L., BAGGENSTOSS, A. H., AND WEIR, J. F.: Parenchymal Calcification of Kidneys in Patients with Duodenal Ulcer. Am. J. Clin. Path. **22:** 843–854, September 1952.
3. BURNETT, C. H., COMMONS, R. R., ALBRIGHT, F., AND HOWARD, J. E.: Hypercalcemia Without Hypercalcuria or Hypophosphatemia, Calcinosis and Renal Insufficiency; Syndrome Following Prolonged Intake of Milk and Alkali. New England J. Med. **240:** 787–794, May 19, 1949.
4. DWORETZKY, M.: Reversible Metastatic Calcification (Milk Drinker's Syndrome). J.A.M.A. **155:** 830–832, June 26, 1954.
5. KIRSNER, J. B., AND PALMER, W. L.: Alkalosis Complicating the Sippy Treatment of Peptic Ulcer. Analysis of 135 Episodes. Arch. Int. Med. **69:** 789–807, May 1942.
6. SNAPPER, I., BRADLEY, W. G., AND WILSON, V. E.: Metastatic Calcification and Nephrocalcinosis from Medical Treatment of Peptic Ulcer. Arch. Int. Med. **93:** 807–817, June 1954.
7. WERMER, P., KUSCHNER, M., AND RILEY, E. A.: Reversible Metastatic Calcification Associated with Excessive Milk and Alkali Intake. Am. J. Med. **14:** 108–115, January 1953.

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SUMARIO

Manifestaciones Roentgenológicas del Síndrome de los Bebedores de Leche

Comunícanse 2 casos del "síndrome de los bebedores de leche," con calcinosis metastática e insuficiencia renal crónica. Ambos enfermos describieron historias de excesivo consumo de leche durante un período prolongado de tiempo.

El típico aspecto roentgenológico es de depósitos calcíficos en los tejidos subcutáneos, por lo general en la proximidad de las articulaciones. No hay alteraciones concomitantes en el tejido óseo.

La explicación del síndrome que se ofrece aquí es la siguiente: La sangre se satura de calcio y fósforo, que se precipitan en los tubos y el parénquima renales. Si existe alcalosis, los riñones excretan una cantidad mayor de ácido. A consecuencia de ello, aumenta la velocidad de la precipitación de las sales cálcicas en el riñón. Una vez que sobreviene insuficiencia renal, la excreción de calcio tiende a fijarse y las concentraciones séricas de ambos cationes permanecen en el punto de saturación. El resultado es calcinosis metastática y más nefrocalcinosis, con perpetuación del ciclo. La eliminación de la leche de la alimentación puede rebajar a lo normal el calcio y el fósforo séricos y hacer virar la calcinosis metastática, pero no invertir mayor cosa la insuficiencia renal.

Cobalt 60 Beam Therapy: Three Years Experience at Montefiore Hospital (New York)[1]

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RADIATION in the supervoltage range offers distinct advantages over conventional 200- to 400-kv radiation for the treatment of cancer. The cost and maintenance of supervoltage x-ray equipment, however, is prohibitive for small cancer centers. The cobalt 60 beam therapy unit in use at the Montefiore Hospital is a simple, relatively inexpensive, and reliable apparatus for the production of gamma rays equal in penetration to x-rays produced by a 3-MEV machine. A lead, steel-lined drum, about 2 feet in diameter and 4 feet high (Fig. 1), holds the radioactive cobalt. In front of the source is a hollow cone containing mercury, which absorbs the radiation when the machine is not in use. The mercury is pumped out by remote control from the control room when a patient is to be treated. Should the power fail or the door of the treatment room be opened, the mercury will return by force of gravity into the cone. The size of the field is regulated manually by means of two levers which adjust the position of four lead blocks at right angles to one another.

The personnel operating the Montefiore cobalt unit, who are monitored continuously by film badges and pocket dosimeters, receive about 1 mr a day. Thus, the operation of a cobalt 60 unit is as safe as that of an x-ray machine.

The advantages of supervoltage over conventional radiation are purely physical. Because of increased penetration, the depth dose is greater. Thus, the dose at 10 cm. depth for a 10 × 10-cm. field is 35 per cent of the surface dose with 200 kv, h.v.l. 1.5 mm. Cu; with cobalt 60 it is 56 per cent. In Figure 2 is shown a comparison of cobalt 60 and 200-kv x-rays for a dose of 5,000 r delivered through three ports. With cobalt 60 the skin receives 4,000 r and the underlying tissues 3,500 r. With 200 kv the skin and underlying tissues must be given 6,500 to 7,500 r, which is beyond tolerance limits. Because the tendency to side-scatter is less with cobalt, the volume of normal tissue irradiated is smaller, resulting in less constitutional disturbance. Skin damage is considerably reduced, and absorption in bone is greatly decreased. Cobalt 60 can therefore be used to treat a tumor underlying normal bone with less danger of bone necrosis.

Since the installation of the first high-intensity cobalt 60 beam therapy unit in the United States, at Montefiore Hospital, a number of such machines have been set up in various cancer centers in this country. We therefore consider it worthwhile to record at this time some of our observations on patients treated with this unit in the past three years.

METHOD OF IRRADIATION

The method by which cobalt 60 beam therapy is applied is most important. The services of a radiation physicist are essential, since accurate dosage planning and beam direction are integral parts of treatment. For the radiation to be most effective, with the least damage to healthy tissue, the rays must be so directed that they strike the tumor from several ports of entry.

There are three steps in the preparation of a plan of irradiation. The first is the exact localization of the growth and the determination of the volume of tissue to be irradiated. For example, after the tumor has been located roentgenographically, the following procedure is followed for all head, neck, and chest lesions which can be

[1] From the Department of Radiotherapy, Montefiore Hospital, New York, N. Y. Presented at the Forty-first Annual Meeting of the Radiological Society of North America, Chicgao, Ill., Dec. 11–16, 1955.

treated with the patient in the erect position. A light plaster-of-paris cast is made of the portion of the body containing the growth. On this cast special tapes with lead markers for localization are placed on the cast after correction for distortion, the physicist locates two perpendicular axes through the center of the tumor. The second step is field selection. A contour of the cross section of the body is ob-

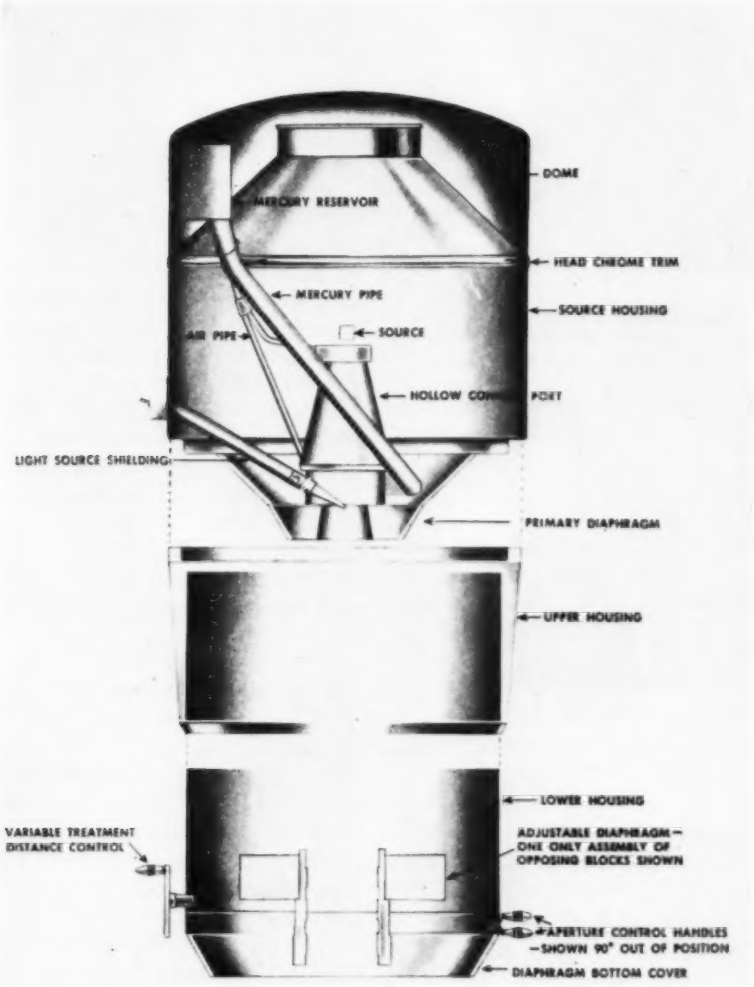

Fig. 1. Cross section of the drum.

anteriorly, posteriorly, and laterally. With the patient in the cast, he is x-rayed in the position in which he is to be treated. Anteroposterior and lateral x-ray films are taken, and on these the radiotherapist outlines the volume of tissue to be irradiated. By identification of the markers tained at the level of the center of the lesion. By applying isodose curves from various angles, the physicist determines the most efficient method of obtaining a uniform treatment field, with minimal damage to important structures such as eyes, spinal cord, etc. The third and final step

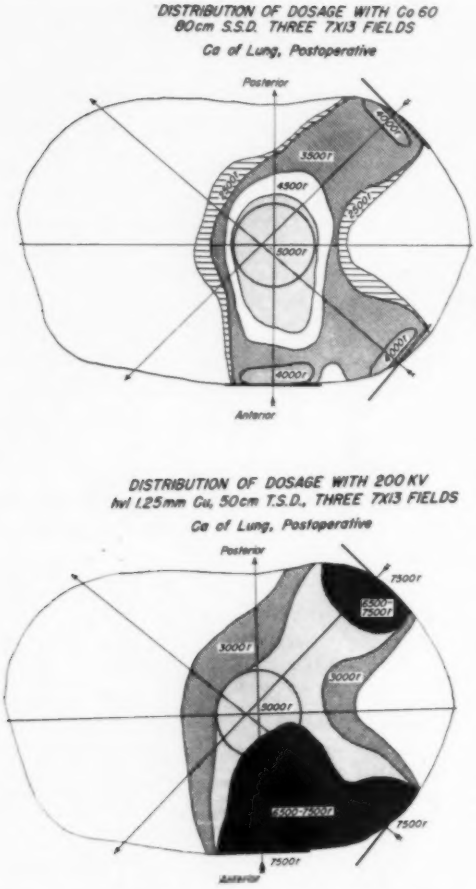

Fig. 2. Comparison of cobalt 60 and 200 kv for a tumor dose of 5,000 r.

is beam direction. The plan prepared by the physicist is discussed with the radiotherapist and, if it is approved, the center of the ports of entry and exit are marked on the cast (Fig. 3).

The cast is worn during each treatment, the machine being so positioned that the Lucite cone fits into the center of the port of entry and the back pointer fits into the center of the exit port, with the result that the beam is always angled in the same direction (Fig. 4). The physicists have also devised a method of obtaining films to make sure that the tumor is being irradiated as planned, using the cobalt 60 source as a diagnostic x-ray tube.

To minimize the skin effect, rotation therapy of the vertical type is utilized in suitable cases. The patient is so positioned that the center of the tumor is at the center of rotation. Sometimes movement of the patient back and forth through a section of an arc is substituted for a complete revolution, in order to spare an area which should not be irradiated. Rotation therapy has proved very useful in carcinomas of the head and neck, esophagus, bladder, and uterus.

The overall period of treatment for most patients is five to seven weeks. Dosage varies. It is limited neither by the constitutional effect of the radiation nor by the skin reaction, but principally by the tolerance of normal tissues in the field of irradiation. We have found that with treatments of five to seven weeks duration, intra-oral, laryngeal, and pharyngeal lesions may be given 6,000 to 7,000 r, carcinoma of the stomach and upper abdominal lesions 4,000 to 5,000 r, pelvic cancers 5,000 to 6,000 r, and carcinoma of the bladder 5,000 to 7,000 r. The lower dosages are used for large lesions, where the best one can hope for is palliation.

REACTIONS

Constitutional effects are minimal even with irradiation of large volumes of tissue in the chest and pelvis. For intra-oral and intracranial lesions, reactions are almost non-existent or, at most, mild. Nausea may be a problem in treatment of disease in the upper abdomen, as in the stomach, liver, pancreas, etc. When present, however, the reaction is milder than that experienced with conventional radiation and can be controlled by Thorazine or pyridoxine intramuscularly or by mouth, or by any of the other preparations used for radiation sickness.

Local Tissue Reactions: Intra-oral and intravaginal mucous membrane reactions are better tolerated, probably because they are not associated with severe skin reactions. Irradiation of the mediastinum frequently leads to dysphagia, the result of radiation esophagitis. Decreasing the dose

Fig. 3. Knitting needles demonstrating ports of entry and exit.
Fig. 4. Patient about to be treated. Lucite cone fits into center of port of entry and the back pointer fits into the exit port.

for short periods of time and limiting food intake to fluids will overcome this difficulty. In pelvic irradiation, diarrhea and rectal and vesical tenesmus, due to radiation proctitis and cystitis, occasionally interfere with treatment. Temporary reduction of dosage, plus administration of belladonna, gantrisin, or opium, as indicated, will control these complications.

Skin reactions in cobalt beam therapy are less severe than in conventional irradiation. In our experience, only mild erythema and bronzing were observed with large fields and total doses as high as 5,500 to 6,000 r at 4 mm. below the upper surface of the skin, and total dosages of 4,500 to 5,000 r at the skin. In some regions, however, the skin reaction is slightly more marked, as for example in areas overlying the sternum and lower pelvis. Wet desquamation was noted in a few instances.

Epilation is common with doses above 2,000 r. In most instances, regrowth of hair is observable within a few months.

Blood: Marked alteration in the red count, white count, platelets, or differential count is rare when small tissue volumes are irradiated.

SELECTION OF CASES

The majority of patients selected for cobalt beam therapy had advanced malignant disease. Some had been found inoperable on surgical exploration. Others, having undergone radical surgery, were referred because of inoperable recurrences. A few patients had been treated by conventional irradiation and were selected for cobalt therapy because of persisting disease. Except for isolated instances, pathologic proof of cancer was obtained before treatment was begun.

CARCINOMA OF THE LUNG

Treatment was given to 83 proved cases of inoperable carcinoma of the lung. Eleven patients were still alive six to thirty months postirradiation. In only 6, however, did the primary lesion appear to be arrested (Table I). Fifteen additional patients were markedly improved for eight to thirty months before death from cancer or, in a few instances, from intercurrent disease. In 46 cases, though adequate doses were administered, death ensued shortly thereafter. While the condition of a few patients was temporarily improved, the group as a whole did badly as judged by the survival period. The cause of death often was metastasis to other organs. Eleven patients received insufficient radiation and could not be evaluated.

In almost every patient given an adequate dose, postirradiation changes took

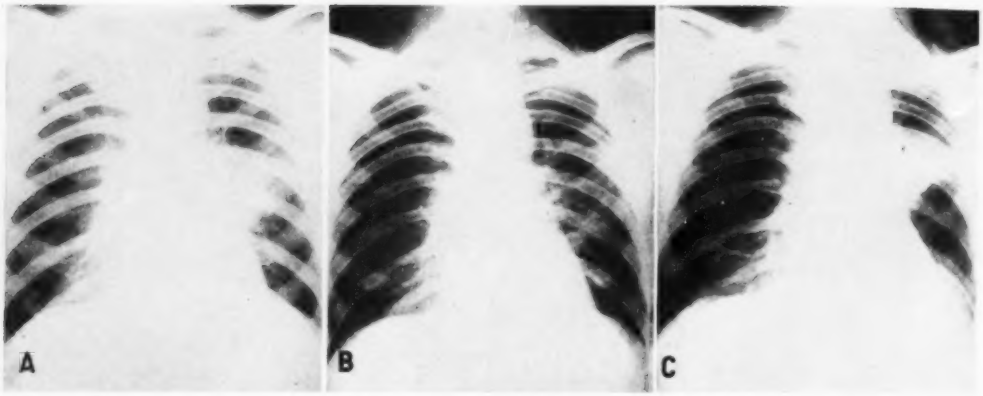

Fig. 5 A. Inoperable carcinoma of the left lung. B. Three months after cobalt 60 beam therapy. C. Postirradiation changes, left hilar region, nineteen months following irradiation.

TABLE I: INOPERABLE CARCINOMA OF THE LUNG. RESULTS OF TREATMENT WITH COBALT 60

	Alive 8 to 30 months	Improved 8 to 30 months, later died	Poor Response	Total
Anaplastic carcinoma	4	5	24	33
Squamous-cell carcinoma	7	7	20	34
Adenocarcinoma		3	2	5
	11 (15.3%)	15 (20.7%)	46 (64%)	72 (100%)

place in the lung (Fig. 5). Injury was minimal as a rule, with few if any clinical symptoms, if the irradiated field was small and limited to the lung periphery. If the field was large and included the mediastinum, symptoms and injury were more likely to be severe. These changes occurred from a few weeks to five months postirradiation. To minimize such trauma, the fields were limited to the smallest size possible for the area involved, and treatment was protracted over five to seven weeks. In 7 patients, fatal hemorrhage occurred during the terminal phase of the treatment or shortly thereafter.

Postmortem examinations were performed in 21 cases in which adequate irradiation had been given. In 2 instances, no tumor was found in the treated area. One of these patients died from extensive metastases; in the other, death was due to hemorrhage from a duodenal ulcer. In 3 cases, the carcinoma showed marked irradiation changes.

Discussion: Patients with pulmonary cancer receiving cobalt 60 beam therapy did not show increased longevity after establishment of the diagnosis as compared to untreated cases. Though there were some exceptions, essentially the figures are not changed. Histology played an important role in longevity. Survival for over a year is much more likely with squamous-cell carcinoma and adenocarcinoma than with anaplastic carcinomas. Occasionally, an undifferentiated lesion exhibited the marked radiosensitivity usually associated with lymphosarcoma. Since pulmonary tumors tend to metastasize especially early, the ultimate result was unchanged. Several patients with carcinoma in an area of active tuberculosis were given full chemotherapy cover during the period of treatment and suffered no undue radiation reactions. For a time, therapy was administered to patients with disease of wide extent and with various complications. It is our conclusion now that poor general condition, extensive intrathoracic disease, widespread metas-

tases, and temperature elevation due to tumor necrosis represent, as a rule, contraindications to radiotherapy. Control of the carcinoma and good palliative effects are more frequently achieved if therapy is restricted to selected groups, namely, for curative effects in patients in good condition, with limited disease; where palliation is the aim; to those with superior vena cava syndrome; to cases of esophageal involvement causing dysphagia, and, where feasible, for relief of such symptoms as severe cough, dyspnea, hemoptysis, and pain. The poor results obtained in both surgical and radiation treatment of carcinoma of the lung serve to underline the fact that this neoplasm, so widely prevalent in our time, has not been significantly controlled by either approach. The disease is widely invasive locally even in those rare cases where distant metastases are not demonstrated terminally.

CARCINOMA OF THE HEAD AND NECK

Treatment was given to 31 patients with lesions of the head and neck, including cancer of nasopharynx, oropharynx, laryngopharynx, tongue, middle ear, and salivary glands.

Nasopharynx: Of 6 patients receiving treatment for nasopharyngeal cancer, 2 were well at the time of this report, after a period of two years. In 1 of the latter, the lesion had extended to the base of the brain when radiation was instituted.

Oropharynx: Seven patients with carcinoma of the oropharynx were treated, and control of the primary disease was achieved in a few. One patient who underwent a radical operation eight months after treatment showed extensive sloughing of soft tissues in the irradiated region.

Laryngopharynx: Treatment was given to 8 patients with advanced laryngopharyngeal disease. One was free of carcinoma for more than two years; the rest did poorly.

Tongue: Five patients had carcinoma of the tongue. With a total dose of 7,000 r, improvement was obtained, but the tumor persisted, when the involvement was in the anterior two-thirds of the tongue. Response was better in lesions located in the base of the tongue and adjacent anterior pillar or pharynx. In 2 cases, the primary lesion disappeared.

Salivary Glands: One patient with recurring adenocarcinoma of the parotid gland was treated following incomplete surgical removal of the recurrence. She was free of disease twenty months following irradiation.

Discussion: When the cobalt 60 beam therapy unit at Montefiore Hospital was installed, we had no special criteria for the selection of suitable head and neck cancers for treatment. Many patients with advanced disease were irradiated for possible palliation. Our results in this category are therefore poor. With supervoltage radiation, however, the nasopharynx and oropharynx can easily be given the large doses necessary to control carcinoma. Discomforts of treatment such as the severe skin reaction are minimal. Necrosis of the mandible, previously encountered in 200-kv therapy to tonsillar and intraoral lesions, is avoided. As a result of better dosage planning, the possibility of radiation injury to the cervical cord is diminished.

A note of warning to surgeons is sounded, concerning the dangers of extensive operative procedures when large volumes of tissue have received high doses of supervoltage radiation. The lack of radiation change in the skin is misleading. Devitalization of tissues is much more marked than with conventional 200- to 400-kv therapy. Several of our patients underwent radical operations following failure of cobalt 60 beam therapy to control the disease. In some cases, extensive necrosis of soft tissues occurred in the irradiated area. Healing was better in surgical procedures of less magnitude.

CARCINOMA OF THE ESOPHAGUS

Of 13 patients treated for esophageal cancer, 4 had tumors in the upper third of the esophagus, 6 in the middle third, and 3 in the lower third. Whenever possible, rotation therapy was employed; treatment

otherwise was by beam direction. Tumor doses were in the 5,000 to 6,000 r range.

In a patient with severe damage to the skin of the neck from x-ray therapy for hyperthyroidism many years previously, a cancer in the cervical esophagus completely disappeared, without recurrence at the end of two years. The remaining 3 patients with involvement in the upper third responded poorly. Of the 6 patients with middle-third lesions, 1 was free of disease for two years; in another, esophagoscopy was negative for cancer but there was obstruction due to a constricting band at the treatment site. The patients with disease in the lower third of the esophagus did badly.

Discussion: Theoretically, supervoltage radiation is the treatment of choice for carcinoma of the esophagus. The poor results obtained again emphasize the fact that it is difficult to control advanced disease by irradiation. Carcinoma of the esophagus is rarely discovered in the early stages. The majority of patients, when they seek treatment, have extensive lesions, incurable by any means. In most cases, the aim of therapy should be palliation of obstruction and dysphagia. Under these conditions dosage will be in a range calculated not to produce fibrosis or other complications. Curative radiation should be reserved for patients in good general condition, with lesions of small extent.

CANCER OF THE BREAST

Three patients, considered unfavorable for surgery, received treatment for cancer of the breast. One with supraclavicular and axillary metastases was given more than 8,000 r to the breast and 6,500 r to the metastatic lesions over a period of seven weeks. Simple mastectomy was performed four months later. The excised breast presented massive fibrosis and hyalinization, and scattered injured tumor cells were noted in the stroma. The patient was well after a period of one year. A second patient with a sizable breast tumor and enlarged axillary nodes received 6,600 r to the primary lesion and 8,000 r to the nodes over a five-week period. Simple mastectomy was performed three months following irradiation. Persistent anaplastic carcinoma was found in the breast. The patient was well, with no clinical evidence of disease, twenty-one months postirradiation. The third patient had an inflammatory carcinoma and was given 7,600 r to the breast in two months, with temporary improvement; her condition subsequently deteriorated, however, and death ensued nine months postirradiation.

A small group of patients received treatment for metastases. As has been observed with conventional irradiation, the response was favorable. The advantage of cobalt 60 beam therapy was that in selected cases, when the condition of the patient was good and the metastatic lesion dominated the clinical picture, intensive therapy could be given with a minimum of general and local reactions.

Discussion: With supervoltage irradiation, larger doses can be delivered to the primary growth in the breast and to the regional lymphatics with less damage to the skin. This procedure, however, is not an alternative to surgery. Except for an occasional localized radiosensitive tumor, it is questionable whether normal tissues will tolerate the doses necessary for control of primary carcinoma of the breast. In the two irradiated primary tumors which were subsequently removed, considerable destruction was observed, but microscopically carcinoma was found to persist, after doses of 8,000 and 6,600 r. Postoperative irradiation and treatment to metastases resulted in few general and local reactions. In cases where the McWhirter technic of simple mastectomy and irradiation is considered desirable, the recommended dosage may be exceeded without severe tissue injury, with the possibility of additional improvement in results.

CARCINOMA OF THE CERVIX, FUNDUS, AND OVARIES

Carcinoma of the cervix, the body of the uterus, and the ovaries will be considered together, since treatment by supervoltage

radiation is similar for these categories.

Cervix: Seven patients with advanced carcinoma of the cervix were irradiated. One with Stage III cancer of the cervical stump and another with a Stage II lesion of the cervix were well for eighteen and twelve months, respectively.

Body of the Uterus: Seven patients had corpus carcinoma, and one a leiomyosarcoma. Of these, 1 with a Stage II lesion was well for fourteen months and 1, Stage III, at eighteen months. Another, Stage IV, was improved, but with persisting carcinoma, at six months. The patient with leiomyosarcoma was better for about one year, but death occurred as a result of recurring disease.

Ovary: Nine patients with advanced carcinoma of the ovary responded poorly to cobalt therapy.

Discussion: Further investigation is required for the evaluation of supervoltage irradiation for carcinoma of the cervix and body of the uterus. It is unlikely that it will ever be the primary treatment for Stages I and II of cervical cancer. It is a better method for delivering the chosen dose for Stages III and IV, with less discomfort to the patient. Our results for advanced disease of the body of the uterus are encouraging.

Most of the ovarian cancers in our series were too extensive for evaluation of cobalt irradiation. This group could not be given effective treatment to all sites of involvement when diffuse intra-abdominal dissemination was present, with or without hepatic metastases. This constitutes the limitation of any kind of irradiation to the diffuse type of ovarian spread.

BRAIN TUMORS

Nineteen patients with the more common varieties of brain tumor were treated. Six cases of glioblastoma multiforme constituted the largest single group. Other types were represented by only 1 or 2 patients each.

Discussion: This material is too limited for the drawing of conclusions. The results in the present series are poor and differ little from those previously obtained with conventional 200- to 400-kv irradiation. Histologically, some of these tumors show considerable variation, ranging from the fully differentiated forms, which are slow growing and run a relatively prolonged course, to the undifferentiated types, which may be fulminating. The biopsy specimen is not always representative of the entire tumor. Considerations other than radiosensitivity are important in treatment of these growths. Large doses are more easily applied with supervoltage technics, with less injury to normal tissues, but the dose must be kept below 5,500 to 6,000 r if late damage to normal brain and spinal cord is to be avoided.

CARCINOMA OF THE DIGESTIVE TRACT

The Rectum and Rectosigmoid: Twenty-five patients with carcinoma of the rectum and rectosigmoid were treated. Some had proved inoperable on surgical exploration. A few had inoperable recurrences; others had metastasis to regional nodes or extensive intra-abdominal involvement and ascites. Fourteen (56 per cent) did not benefit from the treatment; 11 (44 per cent) were improved. Four were still living after six to thirty-one months. Three responded well initially, but died six to twelve months following irradiation. Improvement consisted of relief of hemorrhage and pain, disappearance of ascites (1 case), shrinkage but not disappearance of rectal and rectosigmoid masses, and improvement in the general condition.

Carcinoma of the Stomach: Four patients with gastric carcinoma were treated. Two extensive anaplastic carcinomas which had metastasized to the liver decreased in size but symptoms recurred about one month after irradiation, with death soon thereafter. A patient who had undergone subtotal gastrectomy for scirrhous carcinoma was irradiated for apparent involvement of lymph nodes, which were not resectable. He was doing well one year after treatment.

Carcinoma of the Pancreas: Of 3 patients with pancreatic cancer, 1 showed improvement over a six-month period following a

tumor dose of 5,600 r, but skeletal metastases subsequently developed. The second patient did poorly; the third has been lost to follow-up.

Carcinoma of the Gallbladder: Two patients with cancer of the gallbladder treated with total doses of 5,000 r did poorly and died.

Carcinoma of the Liver: One patient with a hepatoma received 5,000 r and had no complaints eleven months after treatment. The size of the liver was unchanged.

Discussion: To facilitate discussion, the gastrointestinal carcinomas have been divided into two groups, those situated in the upper half of the abdomen (stomach, gallbladder, and pancreas) and those in the lower abdomen (rectum and rectosigmoid). The tumor dose in most instances was 5,000 to 6,000 r over a period of about seven weeks. General and local reactions occurred but, as a rule, this dose was well tolerated. In irradiation of the lower abdomen, the most common complications were radiation cystitis and colitis; treatment to the upper abdomen frequently caused nausea and malaise. The various reactions were usually controlled by proper medication. Few claims, even for temporary palliation, can be made for upper abdominal lesions. Some type of symptomatic relief was obtained in 44 per cent of the lesions in the rectum and rectosigmoid regions. This consisted of arrest of hemorrhage, relief of pain, shrinkage of rectal and rectosigmoid masses, and improved general condition.

SOFT-TISSUE SARCOMAS

Eight patients with soft-tissue sarcomas of various types were treated. Included in this group were patients with incompletely removed infiltrating tumors and inoperable growths, as well as those referred for postoperative irradiation following complete removal of the lesion.

No conclusions can be drawn from our limited material. Of interest is 1 case in which an extensive retroperitoneal fibrosarcoma invaded the bladder and small bowel, with numerous implants on the peritoneum; partial removal of the growth was followed by irradiation, 5,400 r, to the mid-pelvis. Exploratory laparotomy ten months later revealed metastases in the liver, but the pelvis was free of disease. The pelvic mass recurred sixteen months postirradiation. This patient lived for two years following treatment.

Discussion: The response of soft-tissue sarcomas to irradiation is not predictable. It is partially dependent on the degree of malignancy and site of origin. In the past, many such tumors have been considered radioresistant because of the limitations of dosage with conventional 200- to 400-kv therapy. Such restrictions are not a factor in supervoltage irradiation. We have given postoperative tumor doses of 7,000 r to the soft tissues of the thigh with practically no skin reaction and with no late damage in cases observed one to two years. The soft tissues of the extremities will support even larger doses, if indicated, provided treatment is to limited volumes.

MISCELLANEOUS

Included in a miscellaneous category are lymphoblastomas and metastatic lesions of various organs from primary tumors not mentioned in the previous discussion. In most of these cases, the goal was palliation for a major site of involvement. When the general condition was good, and disease in other locations did not create serious problems, relief was obtained. Unfortunately, the lesions were far advanced in many instances and the patients died.

CONCLUSION

Cobalt 60 beam therapy is a practical and valuable addition to the treatment of cancer. Its field of usefulness is greatest for deep-seated lesions. Minimal skin reactions in relation to the high depth dose, low absorption by bone, and mild constitutional effects due to low integral dose are all distinct advantages over conventional irradiation. Although our material was poor, in so far as it consisted principally of advanced cancer, results were encouraging in cancer of the lung, the head and neck,

and the cervix and body of the uterus. Patients treated for control of symptoms from metastases responded well. It is hoped that results will improve for inoperable carcinoma of the breast. Response was poor for glioblastoma multiforme. For the treatment of astrocytoma, medulloblastoma, and other less common gliomas, large tumor doses can be administered with only slight risk of permanent epilation. The response of gastrointestinal tumors was generally poor, though symptomatic improvement was marked in some cases of inoperable or recurrent carcinoma of the rectum and rectosigmoid regions.

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SUMARIO

Terapéutica con el Haz de Cobalto 60: Tres Años de Observación en el Hospital Montefiore (Nueva York)

Preséntanse aquí las observaciones realizadas a usar para terapéutica durante unperíodo de tres años el aparato de haz de cobalto 60 en el Hospital Montefiore (Nueva York). Este dispositivo es un aparato sencillo, relativamente barato y seguro para la producción de rayos gamma de penetración igual a la de los rayos X producidos por un aparato de 3 Mev. Se considera que su mayor utilidad radica en el tratamiento del cáncer profundo. Por haber menos tendencia a dispersión lateral con el cobalto 60, el volumen del tejido irradiado es menor, dando esto por resultado que las reacciones cutáneas son mínimas, la absorción ósea es baja y los efectos constitucionales son leves.

Se describen la construcción y el funcionamiento del aparato. Bosquéjanse los varios pasos que conducen a la formulación de un plan de radioterapia para cada enfermo, con la ayuda de un radiofísico. En los casos apropiados, se emplea la rototerapia vertical. En la mayor parte de los casos, el período de tratamiento dura de cinco a siete semanas; la dosificación varía, fundándose principalmente en la tolerancia de los tejidos normales

Los casos tratados comprendieron cáncer pulmonar, de la cabeza y del cuello, cáncer esofágico, cáncer del cuello y del fondo uterino y de los ovarios, tumores cerebrales, cánceres de las porciones superior e inferior del abdomen y sarcomas de los tejidos blandos.

Aunque el material se considera malo por constar mayormente de casos avanzados, los resultados fueron alentadores en el cáncer del pulmón, de la cabeza y del cuello y del útero. También fué favorable la respuesta al tratamiento dirigido al dominio de los síntomas derivados de lesiones metastáticas. Espérase que los resultados mejoren en el carcinoma inoperable de la mama. La respuesta del glioblastoma multiforme al tratamiento fué mala; para el tratamiento del astrocitoma, del meduloblastoma y de otros gliomas menos frecuentes, cabe administrar grandes dosis tumor sin correr más que leve riesgo de depilación permanente. La mejoría sintomática fué notable en algunos casos de carcinoma inoperable o recurrente del recto y de las regiones rectosigmoideas; los resultados en los tumores gastrointestinales fueron en general malos.

Statistical Appraisal of the Use of Radioactive Iodinated Human Serum Albumin for the Detection of Liver Metastases[1]

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COMMUNICATIONS were published in 1953 by Stirrett, Yuhl, and Libby (11, 12) concerning a technic utilizing radioactive iodinated human serum albumin for the diagnosis of carcinoma metastatic to the liver. The authors found the method to have an accuracy of 95 per cent for differentiating livers containing metastases from those free of tumor. Because of the importance of this work, and because of the unusually high degree of reliability reported by the original authors, a similar study was set up at the Presbyterian Hospital (New York). The object was to test the method in a manner satisfactory for statistical analysis, on the basis of surgically verified cases.

METHOD

The technic described by Stirrett, Yuhl, and Libby (11) was followed closely. The material employed was radioactive iodinated human serum albumin (I^{131}HSA) prepared at Abbott Laboratories. This preparation has been extensively utilized and its properties are now fairly well known (1–3, 6–9, 13). The sterile solution is received in vials and each cubic centimeter contains 0.3 to 0.7 millicurie of the I^{131} bound to approximately 10 mg. of human serum albumin.

Because approximately 3 to 5 per cent of the I^{131} is dialyzable (1), it is necessary to saturate the thyroid gland with inorganic iodide to minimize the uptake of radioactive material. Accordingly, each patient received ten drops of Lugol's solution three times a day for three days during the performance of the study. Routine measurement over the thyroid gland showed no significant uptake of the radioactive material.

Each patient received an intravenous injection of 300 microcuries of I^{131}HSA. Twenty-four and forty-eight hours after the injection the counting procedure was performed. The patient was placed supine on an examining table and 42 points were marked on the torso with indelible ink through a perforated guide. The perforations were 5 cm. apart, and the guide was so placed that the same point (point No. 18) coincided with the surface projection of the tip of the xyphoid process in each case. A drawing was made of each patient, on which the surface landmarks of the torso, the rib cage, the edge of the liver (if palpable), and any abdominal masses were sketched. The actual readings were placed directly on this drawing (Fig. 1).

The counting was performed with a Nuclear Research Corporation scintillation counter, shielded on the sides by 0.5 inch lead and collimated with a lead cone 4.1 cm. in length, with an aperture of 1.25 cm. diameter. On each counting day the counter was standardized and background readings were taken. An adjustable stand held the counter perpendicular to the long axis of the body and in contact with the skin at each point. Sufficient counts were made over each point so that the counting error was not more than ± 3 per cent. The counts per minute were recorded. On the average, slightly more than an hour was required to count each patient.

METHOD OF STATISTICAL ANALYSIS

The twenty-four and forty-eight-hour counts were considered separately, but in

[1] From the Departments of Radiology and Biostatistics, College of Physicians and Surgeons, Columbia University, and from the Radiologic Service of the Presbyterian Hospital, New York, N. Y., and the Radiologic Research Laboratory, Columbia University. Accepted for publication in June 1955.

[2] This work was done in part while Dr. Madell was a Clinical Fellow, American Cancer Society.

an identical fashion. The count over each of the 42 points was recorded in terms of counts per minute, after the daily background had been subtracted. The sum of the recorded values was divided by 42 to obtain the mean of the counts for each patient on each counting day. The individual points were then expressed as percentages of this mean value, which served as a reference.

The values for each point, derived in the fashion described above, were tabulated for the cases without evidence of intra-abdominal carcinoma or liver metastases, which will be referred to as the normal group. The mean and standard deviations for each point were calculated. A range of two standard deviations to either side of the mean was established as normal, thus theoretically including 95 per cent of the normal values (if the series were large enough). It was decided to consider abnormal any value outside of this range.

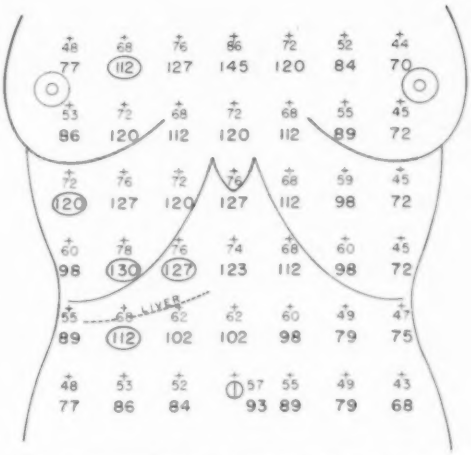

Fig. 1. Reproduction of actual chart of a patient with liver metastases. Only the twenty-four hour readings are given.

Upper numbers in each row represent the actual readings in counts per minute. Numbers immediately below represent the readings expressed as percentages of the mean of all of the readings (mean = 56). High readings are encircled.

CASE MATERIAL

All patients were chosen from the surgical wards of the Presbyterian Hospital. Any patient scheduled for a laparotomy within a week following the counting procedure was considered suitable for the investigation. Patients with and without suspected malignant disease were included. Early in the program several patients were studied in the immediate postoperative period. This practice was discontinued, however, and these patients were excluded from the series, because on superficial examination there appeared to be a localization of radioactivity in the region of the recent incision.

The distribution of I^{131}HSA was observed in 52 patients. Four were excluded from the statistical analysis because of the presence of recent incisions. Four more were excluded because they were never operated upon or because the liver was not examined at the time of operation. This left a total of 44 surgically verified cases for analysis.

Group I: No Intra-Abdominal Tumor or Liver Disease: Patients were placed in Group I according to the following criteria:

(1) There must be no clinical evidence of liver disease.

(2) There must be no evidence of metastatic liver disease and/or intra-abdominal tumor at the time of laparotomy.

(3) The appearance of the liver at operation must be normal.

Of the 44 cases in the series, 21 fell into Group I. They were as follows:

Chronic cholecystitis	5
Duodenal ulcer	9
Gastric ulcer	2
Polyp of colon	1
Peritoneal adhesions	1
Hemangiopericytoma of stomach	1
Thrombosis of aorta	1
No pathology found at operation	1
TOTAL	21

When 10 patients proved to be free of liver disease and without intra-abdominal tumor had been collected, the normal range was calculated as described above under "Method of Statistical Analysis." The data on this series of 10 patients were then put aside in a closed book, which was not opened until the study had been completed. Similar data were accumulated on the

TABLE I: "NORMAL" READINGS

Point No.	Values for First 10 "Normals"				Values for All 21 "Normals"			
	24-Hour		48-Hour		24-Hour		48-Hour	
	Mean	Sigma	Mean	Sigma	Mean	Sigma	Mean	Sigma
1	80	4.7	85	9.8	83	5.6	89	8.7
2	89	4.0	91	3.0	90	6.6	92	8.5
3	113	13	109	3.2	114	12	112	8.5
4	157	18	159	16.7	154	17	150	16
5	127	21	125	13	122	22	117	14
6	90	5.7	87	6.1	90	6.4	90	7.0
7	78	8.0	83	8.2	79	7.1	85	8.2
8	80	5.9	82	9.9	80	5.7	84	8.7
9	92	6.5	92	8.1	92	6.7	94	7.9
10	127	16	126	13.8	128	16	126	14
11	139	12.2	132	14.8	146	14	139	13
12	115	12.4	112	9.5	114	12	114	8.4
13	102	10	101	6.3	100	11	101	8.2
14	84	8.0	88	12.5	84	8.5	91	10.4
15	93	10	95	16.3	94	10	96	12.8
16	113	8.4	112	12.8	110	9.1	111	8.0
17	117	10	116	8.1	117	11	116	8.0
18	121	4.7	120	5.0	122	8.7	120	6.5
19	108	3.2	108	6.3	108	7.9	108	8.3
20	97	3.9	96	8.2	96	7.6	95	5.2
21	86	9.0	83	9.2	85	9.1	83	8.5
22	82	7.1	87	7.1	81	7.2	83	6.8
23	91	7.2	94	11	92	8.6	93	9.0
24	110	4.7	102	5.1	108	7.4	104	7.7
25	118	5.8	114	6.6	116	7.4	113	7.0
26	113	6.6	106	4.0	114	7.1	108	6.6
27	106	4.7	103	4.5	107	7.1	105	7.3
28	91	4.9	94	6.8	92	5.4	95	6.1
29	84	6.5	85	7.7	85	6.3	88	6.8
30	97	4.5	96	3.5	98	7.2	98	5.3
31	100	3.9	101	2.4	101	7.7	102	6.7
32	110	8.3	106	7.5	108	8.0	105	8.5
33	103	7.3	99	7.7	101	7.8	99	5.8
34	96	8.7	90	6.0	93	9.0	90	6.1
35	81	7.5	81	3.7	80	6.5	81	4.6
36	75	5.0	77	3.5	75	5.0	78	5.5
37	88	6.9	87	8.9	87	5.9	85	6.9
38	94	7.0	92	7.5	93	6.7	93	7.2
39	102	4.9	102	6.1	100	6.6	98	8.2
40	92	6.9	94	3.3	91	7.4	94	6.9
41	86	6.2	89	4.5	86	6.9	89	7.9
42	78	9.1	85	8.6	79	8.0	83	6.6

remaining 11 "normal" patients, so that the two groups of "normals" could be compared with each other and yet could be combined to serve as a reference standard for the readings in the other groups.

When the additional 11 "normals" had been gathered, the statistical procedure was repeated for the total group of 21 "normals." As can be seen from Table I, there was a very close agreement between the mean values obtained for the first group and those for the total group.

Group II: Liver Metastases: Seven patients had demonstrable liver metastases at operation (Table II). Six showed high points, *i.e.*, more than 2 standard deviations from the mean. In 1 case (M. Bo.) the high readings were limited to the area of the liver; in 3 cases (N. T., R. T., S. H.) they occurred both over the liver and also over abdominal points unrelated to either the tumor or the liver. One patient (M. B.) gave high readings only over the region of the tumor, which was not in the

TABLE II: GROUP II: PATIENTS WITH LIVER METASTASES

Patient	Site of Primary Tumor	No. of High Readings 24-Hour	No. of High Readings 48-Hour	No. of Low Readings 24-Hour	No. of Low Readings 48-Hour
N. T.	Sigmoid colon (resected)	1	2	1	1
M. Bo.	Sigmoid colon (resected)	3	7	0	1
R. T.	Stomach	4	5	3	1
F. C.	Stomach	0	—	1	—
B. D.	Sigmoid colon	2	0	0	1
M. B.	Stomach	3	2	1	3
S. H.	Rectum	4	0	1	—
Total number of abnormal points		17	16	7	7
Expected number of abnormal points		10.5	10.5	10.5	10.5

TABLE III: GROUP III: PATIENTS WITH INTRA-ABDOMINAL CARCINOMA WITHOUT METASTASIS TO LIVER

Patient	Site of Primary Tumor	No. of High Readings 24-Hour	No. of High Readings 48-Hour	No. of Low Readings 24-Hour	No. of Low Readings 48-Hour
G. L.	Sigmoid colon	2	6	0	1
J. P.	Pancreas	2	3	2	3
R. Q.	Sigmoid colon	1	3	2	4
F. B.	Stomach (with spread to peri-aortic nodes)	3	1	1	3
B. B.	Stomach (with spread to nodes of omentum and celiac axis)	7	4	1	2
P. S.	Rectum	1	1	0	0
N. A.	Ascending colon	1	0	0	0
Total number of abnormal points		17	18	6	13
Expected number of abnormal points		10.5	10.5	10.5	10.5

liver. In another (B. D.) the only abnormal readings were two high points related neither to the liver nor the tumor. In 1 case (F. C.) the only abnormal reading was a single low point over an easily palpable nodular portion of the liver, which at operation was found to be involved by metastatic tumor. Although abnormal points were often duplicated on the forty-eight-hour readings, there was no consistent correlation between the location of such points obtained at twenty-four hours and those obtained at forty-eight hours.

Group III: Intra-Abdominal Carcinoma Without Demonstrable Liver Metastases: In 7 patients intra-abdominal tumors were unassociated with demonstrable liver metastases. Reference to Table III shows that all of this group had abnormally high points. All 7 patients had abnormally high readings over the liver. In 6 these abnormal readings were obtained at twenty-four hours, and in 1 at forty-eight hours.

Group IV: Cirrhosis: Five patients had cirrhosis (Table IV). All gave many high readings, some of which were not over the liver. One patient had, in addition to marked biliary cirrhosis, carcinoma of the common duct and hepatic lymph nodes. One patient had ascites.

Group V: Miscellaneous: This group includes 4 patients with non-neoplastic disease (Table V), in 1 of whom high readings were obtained. The first 2 patients, 1 with pancreatitis and the other with

TABLE IV: GROUP IV: CIRRHOSIS

Patient	No. of High Readings 24-Hour	No. of High Readings 48-Hour	No. of Low Readings 24-Hour	No. of Low Readings 48-Hour
C. R.	7	8	3	2
F. E.	1	4	2	1
E. W.*	4	4	0	2
S. J.	11	6	9	7
E. S.†	5	7	0	0
Total number of abnormal points	28	29	14	12
Expected number of abnormal points	7.5	7.5	7.5	7.5

* This patient had ascites.

† This patient had carcinoma of the common duct, with involvement of the hepatic nodes.

TABLE V: MISCELLANEOUS GROUP

	No. of High Readings		No. of Low Readings	
	24-Hour	*48-Hour*	*24-Hour*	*48-Hour*
Pancreatitis	0	0	0	1
Adenomatous polyp of ascending colon	0	0	1	1
Obstructive jaundice without cirrhosis	0	0	0	0
Echinococcus cysts of liver	2	0	0	0
Total number of abnormal points	2	0	1	2
Expected number of abnormal points	6	6	6	6

adenomatous polyp of the ascending colon, could properly have been included in the "normal" group. In the patient with large echinoccocus cysts of the liver, the only abnormal readings were 2 high points, in the upper chest and the lower abdomen, respectively.

DISCUSSION

Soon after the study was begun, it was realized that the readings expressed as counts per minute were not suitable for comparison. Many variables enter into this value, including the exact amount of radioactive material injected, the somatotype of the patient, the thickness of the subcutaneous tissues, and the relationships of the heart and great vessels to the body surface. Since the object of the study was to obtain a range of normal readings for each point, it follows that the individual readings must be expressed in comparable terms in all patients. An attempt to do this by establishing any one point as a reference leads to difficulty. The reading over the reference point will have an inverse proportionate effect upon all of the other readings. The individual abdominal points are thus immediately excluded from consideration as reference points. The mid-line thoracic readings are the most variable of all, probably because of the variations in the relationships of the heart and great vessels in different subjects, so that they too are unsatisfactory as points of reference.

For the above reasons, it was decided to use the average of the readings as the reference value, as this diminishes the effect of each of the variables listed above. It may be pointed out that this procedure introduces a certain amount of dependence between the 42 points.

In establishing a range of normal readings extending 2 standard deviations to either side of a mean, it is expected that 95 per cent of the normal readings will fall within the normal range (for a large enough series). It is no less expected that 5 per cent of the normal readings will fall outside this range. Actually, correcting for the number of cases in our series and the error of the mean—by reference to the appropriate t-distribution (5)—the probability of another normal falling outside the normal range is 7.1 per cent. If the 42 points are independent, one would expect 1.5 low readings and 1.5 high readings in any patient. Reference to Tables II, III, IV, and V shows that only in Group IV is the number of *low* readings significantly greater than expected, but that in each of Groups II, III, and IV the number of *high* readings is significantly larger than expected (at the 5 per cent level). It would thus appear that the mere presence of intra-abdominal carcinoma causes an abnormal distribution of I^{131}HSA in the abdomen whether or not liver metastases are present. In addition, it was shown earlier that there is no significant selective localization of the abnormal readings over the liver in the group with liver metastases as contrasted to the group without liver metastases. Further, it can be stated that the presence of cirrhosis causes an even greater disturbance of the distribution than does intra-abdominal carcinoma.

Parenthetically, when the second group of 11 normals was compared with the standards set by the first group of 10 normals, there were 46 high points as compared with an expected number of 48.

There is another possible statistical approach which may be of some interest. Consider that the number of abnormal points is not important, but that the occurrence of a single high point anywhere

among the 42 is to be significant, indicating a localized concentration of radioactivity. In order to detect such individuals, it is necessary to re-define the normal range for each of the 42 points in a much more conservative manner. If the points are considered independent, then one must use a range of at least ± 3.6 standard deviations in order to insure that a normal individual would have only a 5 per cent chance of having one or more of his 42 points fall outside the normal range. Interpreting the Group II and III cases on this basis, that is, the group with liver metastases and the group with intra-abdominal carcinoma, it is found that 3 of the 7 cases with proved liver metastases had abnormally high readings over the liver. In each instance, this was a single point, in 2 cases only on the forty-eight-hour count, and in 1 case only on the twenty-four-hour count. Of the 7 patients in Group III, none of whom had evidence of liver metastases at operation, 2 had a single high point over the liver on the twenty-four-hour count and 1 had a single high point over the chest on the twenty-four-hour count.

It is apparent from the above that, even when the strictest criteria are imposed for the definition of an abnormal point, it is still not possible to separate the group with liver metastases from the group without liver metastases when intra-abdominal cancer is present.

CHECK ON THE ADEQUACY OF THE MEASURING METHOD

In order to test the limits within which the measuring procedure should give adequate information, an *in vitro* check was set up. In each of 36 planchettes, 3 cm. in diameter, a solution containing 3.2 microcuries of I^{131} was dried as uniformly as possible. These were then distributed uniformly over a surface of unit density Presdwood, with their centers 5 cm. apart. The pans were then covered by 3 or 6 cm. of the Presdwood and series of readings were taken over 36 points spaced in the same manner as on the skin of the patient. Sometimes the counter was centered over the center of the pans, sometimes over the edges. The mean and standard deviation of the 36 readings were determined for each thickness of Presdwood and for each counter position.

For one of the planchettes, one containing twice as much I^{131} was substituted, and the entire array was measured again; this was also done after similarly substituting one planchette containing three times the average quantity.

When the samples were covered with 3 cm. of Presdwood, it was easy to distinguish the triple concentration; the double concentration produced a high point with a deviation of about 2.5 standard deviations when the counter was deliberately aimed at the edge of the planchette. With 6 cm. of Presdwood, the triple concentration still gave rise to readings which differed by more than 3 standard deviations regardless of the position of the counter, but the double concentration gave readings which were higher by only 2 standard deviations when the positioning was deliberately off-center.

Thus it appears that concentrations of I^{131} three times normal should readily be observed through 6 cm. of tissue, and probably at somewhat greater depths. For differentials of the order of twice normal, fairly superficial deposits would be observed, but deeper ones might be obscured.

The foregoing might account for the absence of high counts over liver metastases if the differential pick-up were small. It does not account for high readings where no metastases exist.

SUMMARY AND CONCLUSIONS

We have explored the feasibility of determining the presence or absence of liver metastases by scintillation counter measurement of the differential concentration of I^{131}HSA, using statistical methods. Direct inspection of the liver and abdomen was carried out in every patient by laparotomy.

There was no significant difference between the number of abnormal readings

in a group with liver metastases and a group with intra-abdominal cancer without liver metastases. However, in the presence of intra-abdominal cancer, primary or metastatic, a significantly large number of abnormal readings was obtained over the abdomen, although the degree of significance is not great.

An *in vitro* experiment showed that the experimental set-up was adequate to detect localized concentrations of radioactive material, if such concentration was as much as three times the normal for the point. For smaller concentrations, the counter gave adequately high readings only if it was centered directly over the deposit. Even then, if more than 6 cm. of tissue intervene, detection becomes uncertain.

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REFERENCES

1. BERSON, S. A., YALOW, R. S., SCHREIBER, S. S., AND POST, J.: Tracer Experiments with I^{131} Labeled Human Serum Albumin: Distribution and Degradation Studies. J. Clin. Invest. **32:** 746–768, August 1953.

2. BERSON, S. A., ET AL: Distribution and Fate of Intravenously Administered Modified Human Globin and Its Effect on Blood Volume. Studies Utilizing I^{131} Tagged Globin. J. Clin. Invest. **32:** 22–32, January 1953.

3. CHOU, S. N., AUST, J. B., PEYTON, W. T., AND MOORE, G. E.: Radioactive Isotopes in Localization of Intracranial Lesions. Survey of Various Types of Isotopes and "Tagged Compounds" Useful in Diagnosis and Localization of Intracranial Lesions, with Special Reference to Use of Radioactive Iodine-Tagged Human Serum Albumin. Arch. Surg. **63:** 554–560, October 1951.

4. DURAN-REYNALS, F.: Studies on Localization of Dyes and Foreign Proteins in Normal and Malignant Tissues. Am. J. Cancer **35:** 98–107, January 1939.

5. FISHER, R. A.: Statistical Methods for Research Workers. Edinburgh, Oliver and Boyd, Ltd., 11th ed., 1950.

6. FREINKEL, N., SCHREINER, G. E., AND ATHENS, J. W.: Simultaneous Distribution of T-1824 and I^{131}-Labelled Human Serum Albumin in Man. J. Clin. Invest. **32:** 138–148, February 1953.

7. MOORE, G. E., CAUDILL, C. M., MARVIN, J. F., AUST, J. B., CHOU, S. N., AND SMITH, G. A.: Clinical and Experimental Studies of Intracranial Tumors with Fluoroscein Dyes, with an Additional Note Concerning Possible Use of K^{42} and Iodine 131 Tagged Human Albumin. Am. J. Roentgenol. **66:** 1–6, July 1951.

8. STERLING, K.: The Turnover Rate of Serum Albumin in Man as Measured by I^{131}-Tagged Albumin. J. Clin. Invest. **30:** 1228–1237, November 1951.

9. STERLING, K.: Serum Albumin Turnover in Laennec's Cirrhosis as Measured by I^{131}-Tagged Albumin. J. Clin. Invest. **30:** 1238–1242, November 1951.

10. STEVENS, C. D., ET AL.: Distribution of Radioactivity in Tumor-Bearing Mice After Injection of Radioactive Iodinated Trypan Blue. Cancer Research **9:** 139–143, March 1949.

11. STIRRETT, L. A., YUHL, E. T., AND LIBBY, R. L.: A New Technique for the Diagnosis of Carcinoma Metastatic to the Liver; Preliminary Report. Surg., Gynec. & Obst. **96:** 210–214, February 1953.

12. STIRRETT, L. A., YUHL, E. T., AND LIBBY, R. L.: The Hepatic Radioactivity Survey. Radiology **61:** 930–934, December 1953.

13. STORAASLI, J. P., KRIEGER, H., FRIEDELL, H. L., AND HOLDEN, W. D.: Protein in the Study of Blood Volume. Surg., Gynec. & Obst. **91:** 458–464, October 1950.

SUMARIO

Avaluación Estadística del Uso de la Seroalbúmina Humana Yodada Radioactiva para el Descubrimiento de Metástasis Hepáticas

Exploraron los AA. la factibilidad de determinar la presencia o ausencia de metástasis hepáticas por medio de mediciones escintilométricas de la concentración diferencial de seroalbúmina humana yodada radioactiva, administrada endovenosamente. Se hicieron numeraciones en cinco grupos de enfermos, todos ellos operados en término de una semana de la numeración: (1) grupo "normal" de 21 sin tumor intraabdominal o afección hepática; (2) 7 enfermos con metástasis hepáticas; (3) 7 enfermos con carcinoma intraabdominal, pero sin metástasis hepáticas descubribles; (4) 5 enfermos con cirrosis; (5) 4 enfermos con varias enfermedades no neoplásicas.

No se notó mayor differencia en el número de numeraciones anómalas entre el grupo de metástasis hepáticas y el grupo de cáncer intraabdominal sin metástasis hepáticas. Sin embargo, cuando existía cáncer intraabdominal, ya primario o metastático, se obtuvo un número significativamente crecido de lecturas anómalas sobre el abdomen, aunque no es alto el grado de significación.

Un experimento *in vitro* demostró que la instalación experimental era adecuada para descubrir concentraciones localizadas de substancias radioactivas, si dicha concentración alcanzaba al triple de lo normal para el punto dado. Para concentraciones más pequeñas, el numerador rendía lecturas adecuadamente altas únicamente si se centraba directamente sobre el depósito. Aun entonces, si intervienen más de 6 cm. de tejido, el descubrimiento se vuelve incierto.

Roentgen Demonstration of Placental Calcification[1]

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PLACENTAL CALCIFICATION, recognizable on pelvimetry films, is one of the phenomena associated with aging and involution of the placenta. This report is concerned with a study of the roentgen patterns of delivered calcified placentas and the correlation of these patterns with the preparturient appearance as seen on pelvimetric films obtained for the usual obstetrical indications.

LITERATURE

Hartley (5) obtained roentgenograms of 252 delivered placentas and found various degrees of calcification in approximately 90 per cent. He believed the phenomenon to be no rarity after the thirty-second week of fetal life. Fleming (3) studied 200 placentas and found 74 per cent to show some degree of calcification. She felt that there was evidence indicating a higher incidence in patients who had received supplements of calcium, minerals, and vitamins. Masters and Clayton (7) demonstrated calcium after the thirty-fifth week in 87.5 per cent of 40 placentas studied.

Calcification of the placenta has also been recognized prenatally. In 1943, Thomas (13) published a lateral roentgenogram of a pregnant uterus, on which placental calcification was plainly visible. The roentgenogram of the placental specimen showed calcifications, heaviest at the periphery of the cotyledons. Linsman and Chalek (6) studied roentgenograms obtained in 100 pregnancies and recognized placental calcification 30 times. The phenomenon was most obvious in patients who had received supplementary calcium and vitamins.

Hartley (5) believed that he was able to identify the site of the placenta 335 times out of 365 cases (98 per cent); 110 (30.1 per cent) of these placentas showed calcification. McDonald (8), Simon (10), and Solomons and Falkiner (11) have also called attention to placental calcification.

ANATOMY

The expelled placenta is described in Gray's *Anatomy* (4) as a discoid mass which has a diameter of 15 to 20 cm. Its thickness averages 3.0 cm., being greater in the center and diminishing rapidly toward the periphery, where it is continuous with the thin placental membranes. The uterine surface is divided into lobules or cotyledons by fissures which extend all the way or partly through the placenta between the maternal and fetal sides.

Fetal and maternal blood currents circulate in the placenta but do not mix. Maternal blood floods the intervillous spaces and bathes the placental villi, which contain the fetal vessels. The delicate walls of the villi separate the systems but permit an exchange of gases, nutritive materials, and waste.

ROENTGEN APPEARANCE OF PLACENTAL CALCIFICATION

When divorced from the confusing overlying shadows of the mother and fetus, the characteristics of placental calcification are obviously easier to define. With this in mind, five specimens of calcified placentas which had been seen on the *in vivo* pelvimetry roentgenograms were obtained and studied roentgenologically. It was then possible to recognize and identify more clearly on the *in vivo* films many of the details thus demonstrated.

The freshly delivered placenta was placed flat on a cardboard film holder and a roentgen image was obtained. The specimens resembled each other strikingly (Fig. 1). The anatomical division into lobules or cotyledons was well shown.

[1] Accepted for publication in August 1955.

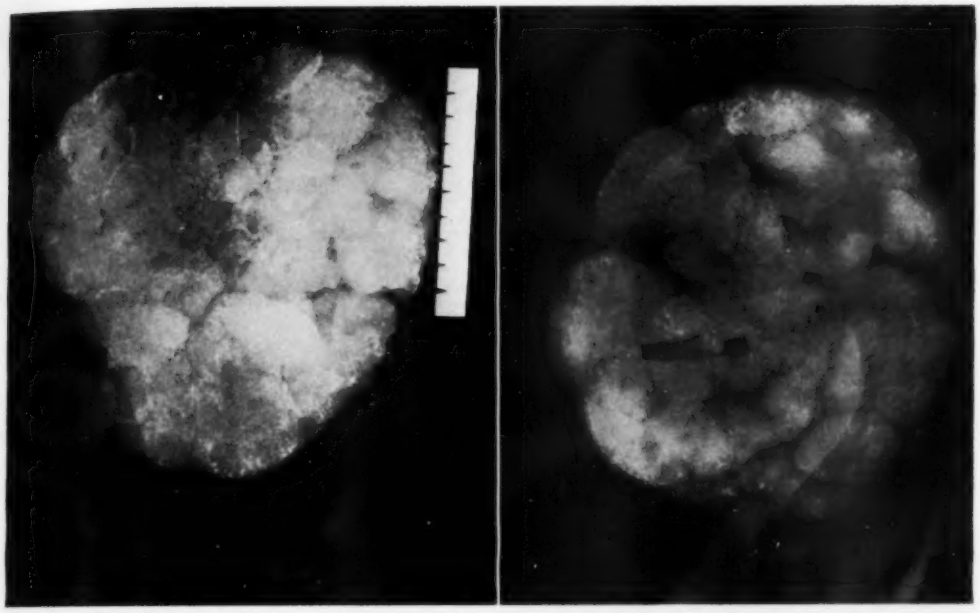

Fig. 1. Two different placentas to illustrate the similarity and constancy of the pattern of calcification. The cotyledons give a lobular character to the placentas. Calcification is greater at the peripheries of the cotyledons.

The calcific phenomenon was greatest at the periphery of the cotyledons. Cross-sectional studies showed this peripheral calcification to be real and not merely suggested by projection through the almost vertical lateral boundaries of the cotyledons. It was not only lateral but was marked at all of the rims. Scattered faint calcific deposits were also noted in the more central portions of the cotyledons. There was a tendency toward greater calcification about the margin of the placenta than toward the middle. The edge was often calcified in a wedge-like fashion.

An attempt to study the finer details of this phenomenon was made by magnifying the images approximately three times (Fig. 2). Further useful enlargement was prevented by the film grain. The striking similarity of the specimens previously noted was duplicated in the appearance on

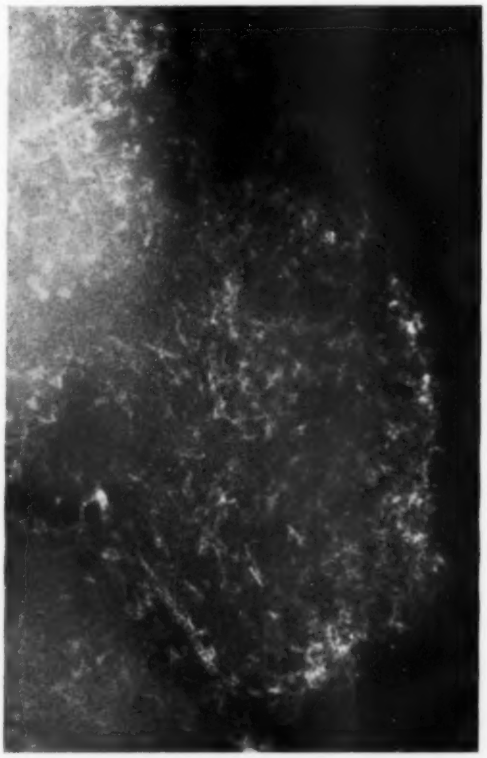

Fig. 2. Enlargement of a cotyledon to show the delicate lace-like pattern of calcification and the tendency to greater calcification both at the periphery of the cotyledon and the placental rim.

Fig. 3. The delicate reticular pattern of calcification is seen in this lateral view of the pregnant uterus. The crescentic shadow lateral to the rib cage is the placenta. The visible epiphysis at the upper end of the tibia usually indicates a fetal age of at least forty weeks.

magnifications. Except for the degree of calcification—and even this was not too dissimilar—the specimens were indistinguishable. The delicate, lace-like, reticular pattern was somewhat reminiscent of fine lung architecture.

Having studied the detached placentas, it was then possible to identify many of their more detailed anatomical features on the pelvimetry films. The fine, lacy, reticular pattern could be defined in almost all instances where calcification was seen. This was especially apparent in the lateral projection, where there were fewer overlapping images (Fig. 3). The shape of several of the cotyledons could be discerned in many of the views (Figs. 4 and 5). Some previously unexplained calcific shadows were identified as portions of cotyledons. The wedge-shaped calcification of the edge of the placenta helped delineate its limits on the pelvimetry films (Fig. 5). In at least one instance, the calcification assumed the form of a long streak. In every case the increased density caused by the calcium led to easier

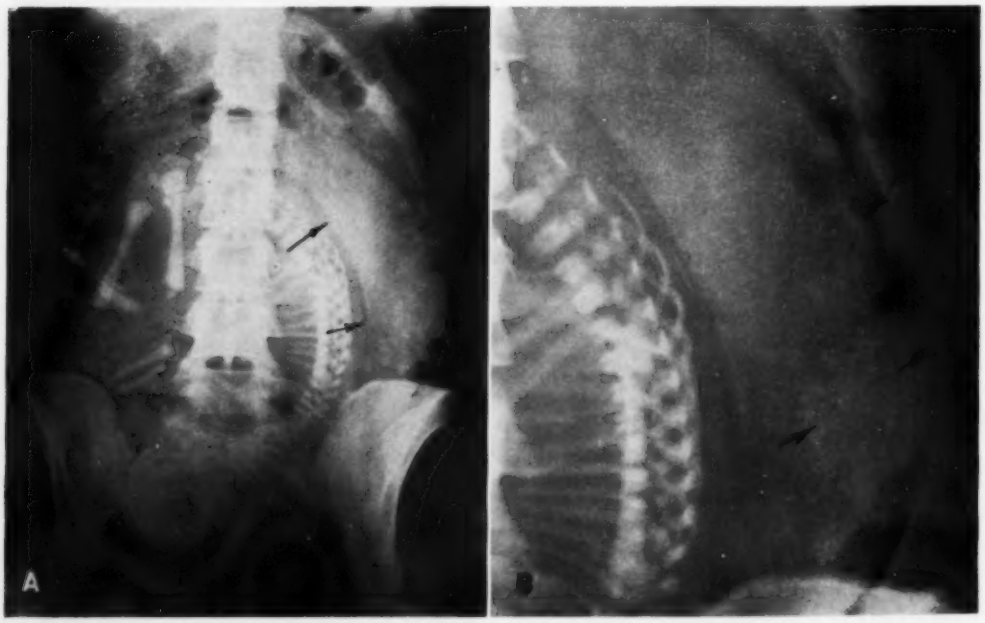

Fig.4. A. The soft tissue shadow behind the fetal spine is the placenta. Calcification within this shadow gives certainty to this opinion. B. Detail view of A. The patterns of calcification suggest the outlines of cotyledons. These structures are more clearly shown on the original film.

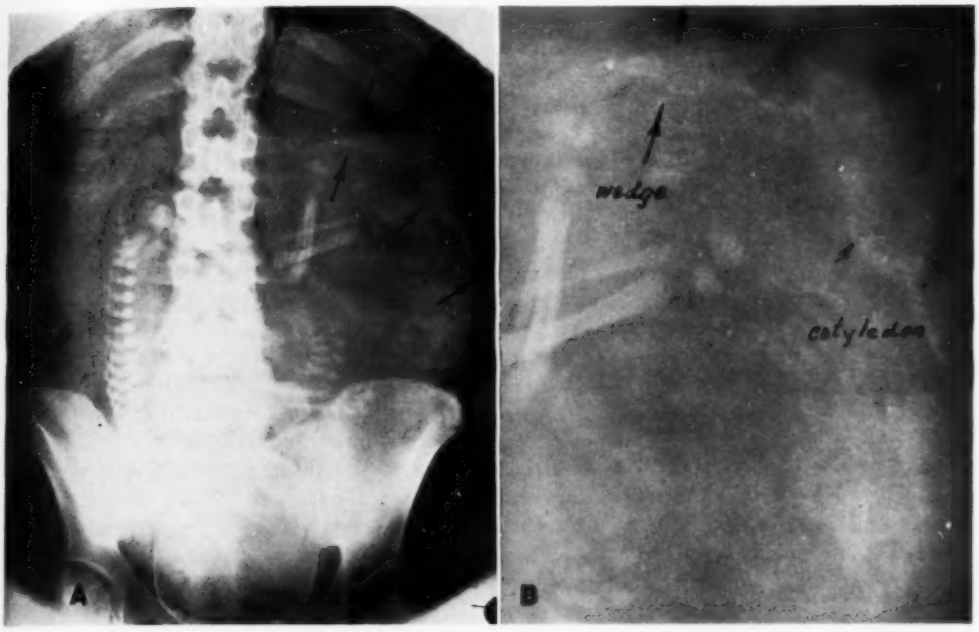

Fig. 5. A. The calcified placenta may be recognized in the left upper quadrant. The feet of the fetus indicate the position. This is a postero-anterior view. B. Detail view of the placenta. Note the wedge-like calcification delineating the upper limits of the placenta. Several oval negative shadows within the placenta outline cotyledons. The fine lace-like detail of the calcification is also suggested.

identification of the placenta. In some cases, although no specific pattern could be seen, the placental shadow was so dense as to suggest unseen calcification.

In the lateral projection the placental shadow is usually easily identified and the calcification within it is a secondary matter for recognition. In the postero-anterior projection, however, it is the calcification itself which often draws attention to the placenta.

Differentiation from other calcifications is usually not necessary. The discoid or crescentic soft-tissue shadow within the outline of the uterus identifies the placenta, and the calcification within it matches the findings described in the specimen studies.

DISCUSSION

The process of calcification appears to be a part of the complex biochemical changes related to placental aging. In itself it has not been found to adversely affect either the mother or fetus. To this extent it is fairly harmless, but not necessarily normal.

Albright and Reifenstein (1) refer to the appreciable depletion of maternal calcium stores in the last two months of pregnancy. Folklore belief that it costs the mother a tooth for each child is descriptive of the same mechanism. As suggested above, placental calcification is believed to be more common in women who have had supplementary calcium and vitamins. Conversely, those with poor calcium intake are less likely to show calcification. If this is true, it implies a mobile reservoir of calcium rather than a pathologic deposition. Earlier in pregnancy at least, Schönig (9) and Wislocki and Dempsey (14) have shown progressive diminution of deposited calcium, suggesting a physiologic rather than a pathologic mechanism.

Deposition late in pregnancy may be of degenerative origin. According to Masters

and Clayton, who studied the phenomenon microscopically, late calcification was seen only where villi had degenerated. Schönig stated that after the fifth month calcium deposits were found in any area where degeneration of villi had occurred and indicated the amount of villous degeneration. Wislocki and Dempsey differentiate between early calcification, which may be physiologic, and late calcification, which increases with advancing placental age and is due to infiltrations of formed calcium occurring irregularly in regressive villi, infarcts, and cell islands, as well as in necrotic foci.

Brehm (2) found placental calcification to be more extensive in women who had received viosterol and calcium and believed that there might be a potential danger in such medication.

There is a wide range of physiologic safety attached to degenerative placental changes. Stander (12) states that the placenta can withstand destruction of at least half of its functioning substance and still maintain fetal life.

The constancy of the pattern of calcification suggests a uniform mechanism. It may furnish a clue to association with a degenerating vascular supply. The distribution coincides roughly with peripheral circulatory mechanisms, where the blood supply is likely to diminish first.

It is possible that, although this type of calcification does not indicate serious malfunction when seen in late pregnancy, if seen earlier, it might suggest disease.

Practically, placental calcification will be useful to the radiologist in permitting an easy confirmation of placental site. One of the first of such cases encountered by the author was a placenta previa, where the placenta was identified from its calcification. Because Masters and Clayton found large deposits of calcium in less than 50 per cent of postmature cases and also found it in normal cases, they believed that this precluded the possibility of using the degree of calcification in the diagnosis of postmaturity. Hartley (5), however, feels that an increase in calcification may yet prove to be a warning sign that the dangers of postmaturity are mounting.

SUMMARY

Placental calcification is not uncommon in the last weeks of pregnancy. It is part of the complex mechanism of placental aging and has no known maleffects on the outcome of the pregnancy.

Roengten studies of the delivered placenta reveal a fine, lace-like, diffuse pattern of calcification. Particularly notable is the increased calcification at the peripheries of the cotyledons. Calcification is also more marked at the rim of the placenta, forming a wedge-like edge which is easily identified. These same placental details may often be recognized on preparturient roentgenograms obtained for the usual obstetrical reasons.

Calcification may be useful to the radiologist for confirmation of the placental site. Roentgen studies of the delivered placenta are recommended to anatomists and pathologists as a convenient method for collating anatomical and pathological findings.

ACKNOWLEDGMENT: The author extends his thanks to Lilla Atkin for the roentgenograms and to Lester Bergman for the photographs.

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REFERENCES

1. ALBRIGHT, F., AND REIFENSTEIN, E. C., JR.: The Parathyroid Glands and Metabolic Bone Disease: Selected Studies. Baltimore, Williams & Wilkins Co., 1948, pp. 1–2.

2. BREHM, W.: Potential Dangers of Viosterol During Pregnancy, with Observations of Calcification of Placentae. Ohio State M. J. **33**: 990–994, September 1937.

3. FLEMING, A. M.: Clinical Significance of Degree of Calcification of Placenta as Demonstrated by X-Ray Photography. J. Obst. & Gynaec. Brit. Emp. **50**: 135–139, April 1943.

4. GRAY, H.: Anatomy of the Human Body. Revised and Re-edited by Warren H. Lewis. Philadelphia, Lea & Febiger, 24th Ed., 1942, pp. 41–49.

5. HARTLEY, J. B.: Incidence and Significance of Placental Calcification. Brit. J. Radiol. **27**: 365–380, July 1954.

6. LINSMAN, J. F., AND CHALEK, J. I.: Placental Calcification in the Roentgen Pregnancy Study. Am. J. Roentgenol. **67**: 267–272, February 1952.

7. MASTERS, M., AND CLAYTON, S. G.: Calcification of the Human Placenta. J. Obst. & Gynaec. Brit. Emp. **47**: 437–443, August 1940.

8. McDONALD, E. J.: Evaluation of Placentography in Late Bleeding of Pregnancy. Radiology **64**: 826–830, June 1955.

9. SCHÖNIG, A.: Über den Kalktransport von Mutter und Kind und über Kalkablagerungen in der Plazenta. Ztschr. f. Geburtsh. u. Gynäk. **94**: 451–465, 1928.

10. SIMON, J.: Calcifications placentaires: étude clinique, histologique, et radiologique. Bull. Fed. soc. gynéc. et obst. **3**: 408–417, 1951.

11. SOLOMONS, E., AND FALKINER, N. M.: Calcification of Placenta. Irish J. M. Sc., March 1946, pp. 99–100.

12. STANDER, H. J.: Williams' Obstetrics. New York, Appleton-Century Co., 8th ed., 1941, p. 763.

13. THOMAS, S.: Diffuse Calcification of the Placenta Demonstrable in Vivo. Radiology **41**: 573–575, December 1943.

14. WISLOCKI, G. B., AND DEMPSEY, E. W.: Histochemical Age—Changes in Normal and Pathological Placental Villi (Hydatidform Mole, Eclampsia). Endocrinology **38**: 90–109, February 1946.

SUMARIO

Descubrimiento Roentgenológico de la Calcificación Placentaria

La calcificación placentaria no es rara en las últimas semanas del embarazo, formando parte del complejo mecanismo del envejecimiento de la placenta y sin ejercer, en lo que se sepa, malos efectos sobre el resultado de la gestación.

Los estudios roentgenológicos de la placenta expulsada revelan un patrón difuso, fino, calado de calcificación. En particular notable es el aumento de la calcificación en las periferias de los cotiledones. La calcificación es también más acentuada en el borde de la placenta, formando un canto cuneiforme que es fácil identificar. Estos mismos detalles placentarios pueden también reconocerse a menudo en las radiografías tomadas antes del parto por las habituales indicaciones tocológicas.

Las calcificaciones pueden resultar útiles para el radiólogo para confirmar el asiento de la placenta. Recomiéndanse los estudios roentgenológicos de la placenta expulsada a los anatomistas y los patólogos como método conveniente para comparar los hallazgos anatómicos y los histopatológicos.

A Roentgen Study of Bone Metastases from Melanoma[1]

HENRY M. SELBY, M.D., ROBERT S. SHERMAN, M.D., and GEORGE T. PACK, M.D.

SOME CANCERS have known proclivities to metastasize to specific organs as determined by the route of dissemination and by the unexplained phenomenon of selective localization. Malignant melanomas are known to disseminate widely, but the extent and incidence of visceral involvement have not been fully appreciated. In the course of treating more than 1,300 patients with malignant melanoma, the Mixed Tumor Service of Memorial Cancer Center (New York) has had a unique opportunity of analyzing the distribution of metastases as determined by postmortem examination. The incidence of metastatic involvement of various organs and tissues is illustrated in the accompanying diagram (Fig. 1). From a study of this scattergram it may be seen that there is no cancer so commonly inclined to widespread dissemination. For example, in proportion to frequency of occurrence, melanoma involves the brain (38 per cent) more often than any other cancer, exceeding even bronchogenic and mammary cancer. Forty-four per cent of patients dying of malignant melanoma have metastatic deposits in the heart, which is a greater incidence of involvement than obtains for any other neoplasm, even rhabdomyosarcoma and liposarcoma, which are known to disseminate to the heart with some frequency. Forty-nine per cent, or practically one out of two patients dying of melanoma, have bone metastases. The great majority of these metastases are silent or obscured by other symptoms and signs predominating in the terminal stages of the disease.

The purpose of the present communication is primarily to discuss the radiographic manifestations of metastatic melanoma of bone. Although such metastases are not frequently encountered by the roentgenologist, it is still necessary for him to be generally acquainted with the appearance that these deposits may present on the radiograph. A survey of the scanty literature dealing with the roentgen findings in this condition revealed several reports, all of which, however, were based on relatively few patients. The most recent, by Wilner and Breckenridge (1), included 5 cases in which they characterized these metastases as predominantly osteolytic. They also summarized the pertinent literature and cited 12 cases having dependable roentgen evaluation of the bone lesions, all

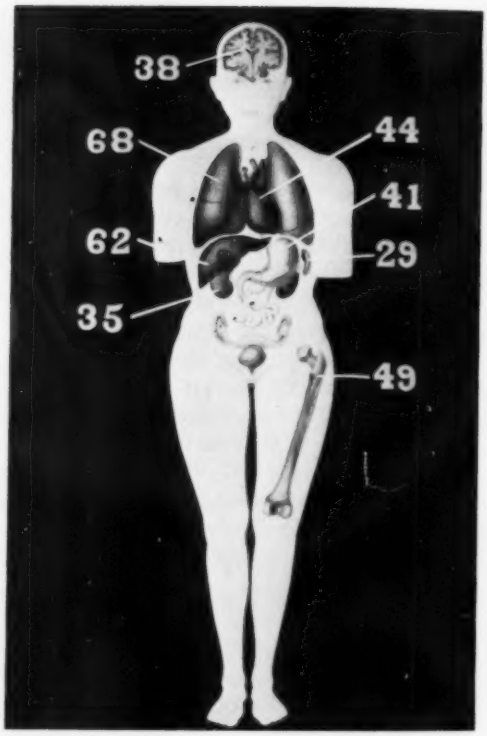

Fig. 1. Topographic chart showing incidence of distribution of metastatic melanoma found on postmortem examination.

[1] From the Department of X-Ray Diagnosis and the Mixed Tumor Service, The Memorial Cancer Center, New York, N. Y. Accepted for publication in August 1955.

of which were described as being largely osteolytic (2–5).

From the considerable volume of melanomas of the Mixed Tumor Service of the Memorial Cancer Center, 33 cases with bone metastases having adequate x-ray film coverage were studied. This provides a sufficient basis, it is believed, to establish the roentgen characteristics of such metastases. Pathological proof was obtained for each tumor but, of course, not every individual bone lesion was proved histologically. In no instance, however, was a second neoplasm known or suspected. The number of bones involved varied from 1 to 12, and the total metastases in each individual from 1 to 12, except for 2 cases with very numerous skull metastases (Fig. 2). Excluding these skull metastases, which were too many to be counted, 90 individual melanoma deposits in bone were studied. Seventeen patients had solitary metastases, although not all of this group had complete skeletal surveys. The location of the single deposits was as follows:

Ribs	6
Skull	4
Pelvis	2
Spine	2
Humerus	1
Tibia	1
Paranasal sinuses	1

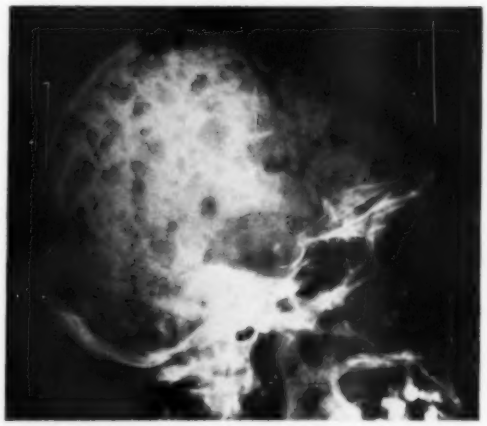

Fig. 2. Multiple osteolytic metastases in the skull, indistinguishable from multiple myeloma or carcinoma deposits.

In the total of 33 cases, the long bones were involved in 6, the flat bones in 27, and the spine in 9. The long bones alone were invaded in 3 instances, the flat bones alone in 19, and the spine alone in 4. Metastases in 2 or more of the above regions were found in 7 patients. The lesions in the long bones were located equally in the diaphyseal and metaphyseal regions. The epiphyses, which were always closed, were never invaded. Metastases in the ribs were about equally distributed between the posterior, mid, and anterior portions.

Fig. 3. Osteoblastic and to a lesser degree osteolytic metastasis in the ilium, with pathological fracture.

Fig. 4. Dense osteoblastic process in multiple vertebrae.

Fig. 5. Eccentrically placed metastasis in the humerus, with calcium deposits in the soft-tissue mass. This has many characteristics of a primary bone tumor.

ROENTGEN FINDINGS

Most of the metastatic lesions were medullary in origin. In 29 patients all the metastases present were osteolytic. In the remaining 4 they were osteoblastic to varying degrees. One of this latter group had a mixed osteoblastic and osteolytic process, with the former element predominating (Fig. 3). In another, a metastasis to a rib showed a mixture of both osteolytic and osteoblastic change. In a third case, there was destruction in the left ethmoid and part of the left frontal bone, along with dense osteoblastic metastases in several vertebrae and several 1-cm. ovoid osteoblastic lesions in the pelvis (Fig. 4). Careful investigation of this patient revealed no evidence of cancer of the prostate and the acid phosphatase level in the blood was normal. The fourth patient had a unique deposit in the ilium, an oval osteolytic lesion showing a definite border of sclerosis around its inferior half. No therapy had been given in this case.

In 16 of the series a soft-tissue component was noted. This varied in size up to 10 cm. in diameter (Figs. 5 and 7). Three cases showed a prominent soft-tissue tumor. One in the skull was associated with a shallow saucerized area of contiguous invasion of the outer table, about 1 mm. in depth. The second was a relatively large soft-tissue mass in the calf of the leg. The tumor invaded both tibia and fibula, and each bone presented a small periosteal reaction. In the third case the metaphyseal region of the humerus was involved, with the tumor mass situated about 75 per cent outside the bone and causing an eccentric area of bone destruction (Fig. 5). In the 4 patients whose facial bones or paranasal sinuses were involved, it was difficult to determine the site of origin of the metastases. One gained the impression that the tumor arose in the soft tissues and destroyed the surrounding bone secondarily. However, the possibility of an origin in the bone itself cannot be excluded (Fig. 6).

The direction of growth of the metasta-

ses was mostly in bone except for the 3 cases in which the soft-tissue element was predominant and 9 others in which the tumor grew both within and outside of bone. In the long bones the metastases were more often asymmetrical than symmetrical, but in the ribs the deposits were usually symmetrical. All the metastases had a more or less ovoid configuration.

Fig. 6. Tumor in the antrum, destroying its walls. This has the roentgen appearance of antral carcinoma.

Usually, no internal structure or pattern was noted. In one instance, however, there was an area of slight production in the peripheral portion of the lesion in a rib. Another deposit showed a few septa (Fig. 7), while in a third there was scattered amorphous calcification in the soft-tissue component. Finally, a metastasis in the metaphyseal region of the humerus contained amorphous flecks of calcification (Fig. 5). The boundary of each lesion appeared either sharp and distinct, somewhat ill-defined, or indefinite. Only one case showed sclerosis or a zone of production in the border of the lesion. With two exceptions in a rib and in a long bone, respectively, both ovoid, osteolytic, and measuring less than 1 cm., all the metastasesca used some destruction of the cortex.

Generally speaking, little periosteal reaction was observed. In most of the instances in which a periosteal change was

Fig. 7. Metastasis with large soft-tissue mass. Septa are seen in its inferior portion.

found, it was minimal and required careful examination for identification. A small reaction was present in a rib deposit. In 1 metastasis to the skull, with a large soft-tissue mass, a slight periosteal density was also noted. There was, in addition, 1 case in which a periosteal change was questionable.

Pathological fractures occurred in 15 patients. Seven involved the ribs. It seems remarkable that there were no fractures in long bones in this series. One such case has been reported, however, by Geschickter and Copeland (2).

The lesions varied from 5 mm. to 18 cm. in diameter, the average being about 3 cm.

It is difficult to say much about the growth rate. The number of cases with coverage over a sufficient time is inadequate for full evaluation of progression rates. One tumor showed no change in two months; on the other hand, several increased in size threefold within the same period. Not enough cases had received treatment to permit any appraisal of the effect of radiation therapy on the metastatic lesions.

SUMMARY

1. Thirty-three patients with histologically proved melanoma metastasizing to bone were studied roentgenographically.

2. The roentgen appearance of bone metastases from melanoma is not specific, but they are usually osteolytic, oval in shape, medullary in location, and show cortical destruction.

3. A few of the metastases in this series presented unusual features of sclerosis and a bulky soft-tissue mass.

4. Melanoma metastases are more likely to occur in flat bones. In somewhat less than half of the cases observed there was a soft-tissue component.

REFERENCES

1. WILNER, D., AND BRECKENRIDGE, R. L.: Bone Metastasis in Malignant Melanoma. Am. J. Roentgenol. **62**: 388–394, September 1949.

2. GESCHICKTER, C. F., AND COPELAND, M. M.: Tumors of Bone. Published by Am. J. Cancer, New York, 1931.

3. HOWES, W. E., AND BIRNKRANT, M.: Melanoma. Review of 32 Cases Admitted to Brooklyn Cancer Institute During 5-Year Period. Am. J. Surg. **60**: 182–189, May 1943.

4. LIVINGSTON, S. K.: Melanoma of the Lumbar Region Without Apparent Skin Manifestation; Case Report. Am. J. Roentgenol. **37**: 46–48, January 1937.

5. RUSSO, P. E.: Malignant Melanoma in Infancy. Report of Three Cases. Radiology **48**: 15–19, January 1947.

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SUMARIO

Estudio Roentgenológico de las Metástasis Oseas del Melanoma

Trienta y tres enfermos que tenían melanoma comprobado histológicamente con metástasis en los huesos fueron estudiados radiográficamente en el Centro Conmemorativo de Cáncer de Nueva York.

El aspecto roentgenológico de las metástasis óseas del melanoma no es específico, pero normalmente son osteolíticas, de forma oval, radican en la médula ósea y muestran destrucción cortical. Algunas de las metástasis de esta serie presentaban características extrañas de esclerosis y tumefacción voluminosa de tejido blando.

Las metástasis melanomatosas son más susceptibles de presentarse en los huesos planos. En algo menos de la mitad de los casos observados, había un componente de tejido blando.

Vertebral Trans-Skeletal Phlebography[1]

MAURICE M. ALBALA, M.D., CLAUDE W. BARRICK, M.D., and EDWARD L. JENKINSON, M.D.

A SATISFACTORY demonstration of the durorachidian veins has seldom been achieved in the living subject. Tori of the Radiological Institute of Bologna University reported on a series of 20 cases (1), showing that the durorachidian venous system could be well delineated by injection of the vertebral spinous processes. It had previously been shown, by trans-skeletal injection, that contrast material readily entered the circulation. In Tori's series, in living patients, injections were made into various thoracic and lumbar spinous processes or into one of the lower ribs. His purpose was to demonstrate the azygos vein and its relation with the intercostal and the external and internal vertebral plexuses, and to show the collateral channels between the superior and inferior vena cava.

MATERIAL AND METHODS

Our interest in this problem arose in an attempt to demonstrate the thoraco-abdominal venous system in living patients, using a simple safe technic, which at the same time would show these veins in sharp contrast. We therefore attempted to duplicate the trans-skeletal technic. Twenty-eight patients were studied by this procedure. This preliminary series was selected at random from a group showing no evidence to suggest venous disease, except for 2 patients with paraplegia in whom no clear-cut venous abnormality was demonstrated.

An ordinary sternal marrow needle was inserted into one of the lower thoracic or lumbar spinous processes. The small marrow needle was found to be preferable because it could more easily be forced through the bone and caused less potential space for leakage around it during the injection. For placement of the needle an awl-like motion is required, which produces a hole large enough to allow leakage of contrast material backward along the needle tract and out into the soft tissues. Due to this leakage a small caliber needle is imperative. The insertion is made after injection of the skin and periosteum with novocain. With smaller needles this is easily accomplished without discomfort. The lumbar spinous processes are larger and more vertical and are, therefore, easier to enter. With the needle in place, prone and lateral films are made in order to demonstrate the needle tip within the spongiosa of the bone. After the films have been examined, 20 c.c. of 70 per cent Diodrast[2] is injected as rapidly as possible. This usually requires four to eight seconds. The patient is warned to expect a rather moderate and transient stinging sensation at the point of injection, as well as a general flushing of the skin. Immediately upon the termination of the injection, a single lateral exposure is made. In several patients, one of the lower ribs was injected. Just prior to completion of the injection and before the exposure, the patient is instructed to take a deep breath and hold it until the exposure is terminated.

In several instances, there was extravasation of a small amount of contrast material into the soft tissues (Fig. 1). This was painful but lasted only a short time, without further untoward reaction. When a lower thoracic spinous process was injected, a variable amount of Diodrast was seen in the complicated network of the durorachidian vein system as well as in several intercostal veins above and below the level of injection. There was always a greater or lesser amount of contrast material in the azygos vein up to its point

[1] From the Departments of Medicine and Radiology, St. Luke's Hospital, Chicago, Ill. Accepted for publication in July 1955.

[2] Supplied through the kindness of the Winthrop Laboratories, Chicago, Ill.

Fig. 1. Injection of 70 per cent Diodrast into the spinous process of the 12th dorsal vertebra. Visualization of the last three intercostal veins and their durospinal branches. The intercostal veins enter the azygos vein, which can be followed along its thoracic course to the superior vena cava.

Fig. 2. Injection of 70 per cent Diodrast into the spinous process of the 2nd lumbar vertebra. Good visualization of the external and internal vertebral plexuses, the first lumbar vein, one intercostal vein, and the origin and thoracic course of the azygos vein.

of entrance into the superior vena cava (Figs. 1–3). When a lumbar spinous process was injected, several lumbar intercostal veins were filled along with an unpredictable number of durorachidian veins (Figs. 4 and 5). In several instances, the inferior vena cava was shown to good advantage (Figs. 4 and 5). When one of the lower ribs was injected, the intercostal and azygos system was strikingly well shown, but the durorachidian veins were not filled (Fig. 6).

DISCUSSION

It has been shown that the vascular bed of the vertebral column is much larger than the circulation requirement of the tissues. Having no valves and an unusually rich anastomosis with other veins, this system is subject to reversals in the direction of the blood flow with changes in the intra-abdominal and intrathoracic pressure, such as occur with coughing or straining (2, 3).

Upon injection of the dorsal vein of the penis in a monkey, most of the contrast material entered the inferior vena cava. After the application of external abdominal pressure, much of the medium passed from the inferior vena cava into the durorachidian veins (2, 3). Theoretically, these vascular connections provide the explanation for an important mode of metastasis of breast and prostatic tumors, cerebral emboli following injection of air into the retroperitoneal space or pneumothorax, and the cerebral extension of bronchogenic tumors.

Vertebral phlebography provides a new means for the demonstration of mediastinal masses with obstruction of the superior vena cava and azygos veins. It may also prove of value in the demonstration of retroperitoneal masses that impinge upon the inferior vena cava. The use of the procedure for the investigation of some of the more obscure lesions of the spinal medulla where there is indirect evidence that a vascular lesion may be responsible is contemplated. Primary lesions of the vertebrae (hemangiomas) may have their circulatory changes clarified.

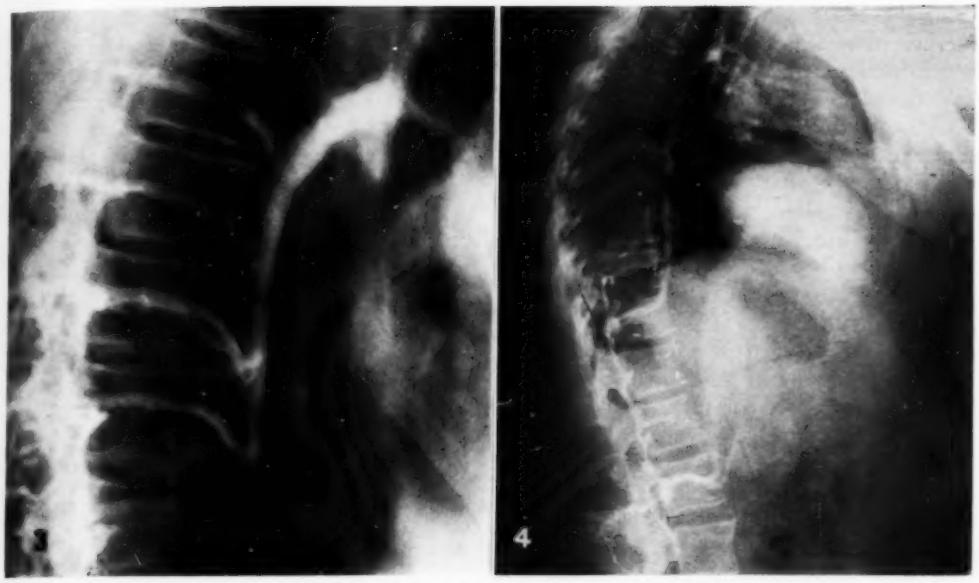

Fig. 3. Injection of 70 per cent Diodrast into the spinous process of the 8th dorsal vertebra. Several intercostal veins are well seen proximal to the injection, and one distal to it. The durorachidian veins and the azygos vein are demonstrated.

Fig. 4. Injection of 70 per cent Diodrast into the spinous process of the 2nd lumbar vertebra. Good visualization of the external vertebral plexus, the 2nd lumbar vein as it enters the inferior vena cava, and the origin and course of the azygos vein. Partial visualization of the lower intercostal veins.

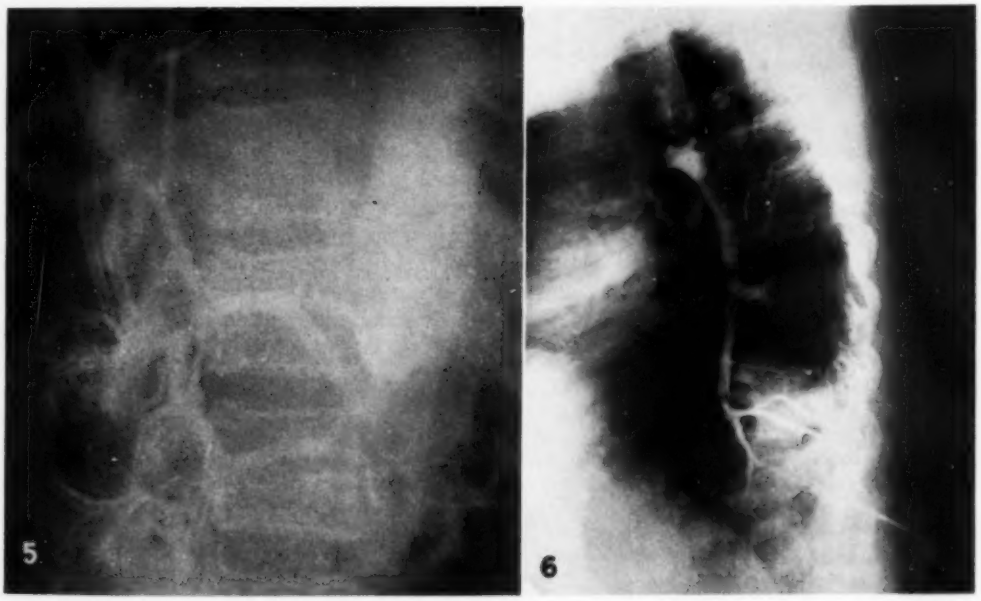

Fig. 5. Injection of 70 per cent Diodrast into the spinous process of the 2nd lumbar vertebra. Good visualization of the external and internal vertebral plexuses, and the 2nd and 3rd lumbar veins as they enter the inferior vena cava.

Fig. 6. Injection of 70 per cent Diodrast into the posterior segment of the 8th rib. Several intercostal veins are demonstrated. The azygos vein can be followed from its origin. Rib injections produce the most satisfactory demonstration of the azygos vein.

The investigation is being carried out further in a series of normal patients in which laminagraphy will be used to clarify the detail of the durorachidian veins. The importance of different phases of thoracic and abdominal pressure changes will be evaluated by a combination of different projections. The combination of this procedure with injection of the sternum or possibly other bone structures in the shoulder or pelvic girdle may clarify obscure conditions.

Our series served to demonstrate the remarkable ease and safety with which the venous system may be filled with contrast material introduced by the trans-skeletal route.

SUMMARY

A simple procedure for visualization of the thoracolumbar veins is presented.

A method of trans-skeletal injection of Diodrast into the spinous processes of the lower dorsal and lumbar vertebrae or lower ribs is described. This method has the advantage of simplicity and safety.

Ordinarily there was a striking demonstration of an unpredictable number of ramifications of the durorachidian veins, the intercostal veins, and the azygos vein. When the 4th and 5th lumbar spinous processes were injected, the inferior vena cava could be demonstrated at its origin.

This procedure may be of value in the investigation of primary tumors of the pelvis, mediastinum, and vertebrae, and some of the more obscure lesions of the spinal medulla.

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REFERENCES

1. TORI, G.: The Radiological Demonstration of the Azygos and Other Thoraco-Abdominal Veins in the Living. Brit. J. Radiol. **27**: 16–22, January 1954.
2. BATSON, O. V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastases. Ann. Surg. **112**: 138–149, July 1940.
3. BATSON, O. V.: The Role of the Vertebral Veins in Metastatic Processes. Ann. Int. Med. **16**: 38–45, January 1942.

SUMARIO

Flebografía Transesquelética Vertebral

El método flebográfico aquí descrito utiliza la inyección transesquelética de Diodrasto en las apófisis espinosas de las vértebras dorsales inferiores y lumbares o las costillas más bajas. Esto proporciona una notable visualización de un número impredecible de ramificaciones de las venas durospinales, intercostales y la acigos mayor. Cuando la inyección es en las apófisis espinosas de la cuarta y la quinta vértebras lumbares, puede observarse la vena cava inferior en su origen.

El procedimiento posee la ventaja de la sencillez y la inocuidad, pudiendo resultar útil en la investigación de los tumores primarios de la pelvis, del mediastino y de las vértebras, y de algunas de las lesiones más obscuras de la médula espinal.

Progressive Diaphyseal Dysplasia (Engelmann's Disease)[1]

EDWARD B. SINGLETON, M.D., JOHN R. THOMAS, M.D., WILLIAM W. WORTHINGTON, and JOHN R. HILD, M.D.

IN 1929, ENGELMANN (1) called attention to a bizarre disease, which he referred to as "osteopathia hyperostotica sclerotisans multiplex infantilis," involving the long bones of an eight-year-old boy. Nine years prior to this, a similar case with identical radiographic findings had been described by Cockayne (2). It was not until 1943, when Riley and Shwachman (3) reported 2 additional cases, that attention was again called to this unusual condition. In 1948 Neuhauser *et al.* (4) published 4 cases, 2 of which had been previously reported (3) under the simpler descriptive title, progressive diaphyseal dysplasia. Since then, several examples have been added to the literature. In view of the perplexing facets of this condition and lack of knowledge regarding its etiology, we offer an additional case with the hope that by the accumulation of enough material some insight into this unusual disease can be obtained.

CASE PRESENTATION

W. R., a white boy of five and a half years (Fig. 1), was admitted to the Texas Children's Hospital on June 7, 1954 because of a peculiar gait. He began walking at eleven months of age and apparently had no difficulty until the age of two years. Development of the unusual gait was insidious and it was first brought to the attention of the parents by persons outside the family. The patient tired easily and frequently complained of ankle pain and leg cramps, but joint swelling was never noticed. He had been examined by several physicians and was considered to have postparalytic poliomyelitis. Radiologic examination of the pelvis and hips had been reported negative. Review of systems was normal except for a history of occasional shortness of breath associated with vague chest pain and tachycardia.

The child was the product of a normal gestation and delivery and at birth weighed 7 pounds. His appetite had always been good, with adequate but not excessive vitamin intake. After the age of two years, however, his weight gain had been very slow. His development during infancy was within normal limits. He walked alone at eleven months and said single words at twelve months. Past illnesses included frequent upper respiratory infections and chickenpox at the age of four years. Tonsillectomy was performed at four and a half years of age, and a few months later a left cryptorchism was repaired. Both parents were in good health and there was no familial history of osseous or neuromuscular disorders. The maternal grandfather and a great uncle were diabetics.

Fig. 1. The patient, aged five and a half years.

On physical examination, the patient appeared thin and undernourished, but alert and intelligent. He walked with a peculiar waddling gait as though he were "stiff at the knees and flat footed." The skeletal musculature was poorly developed and the

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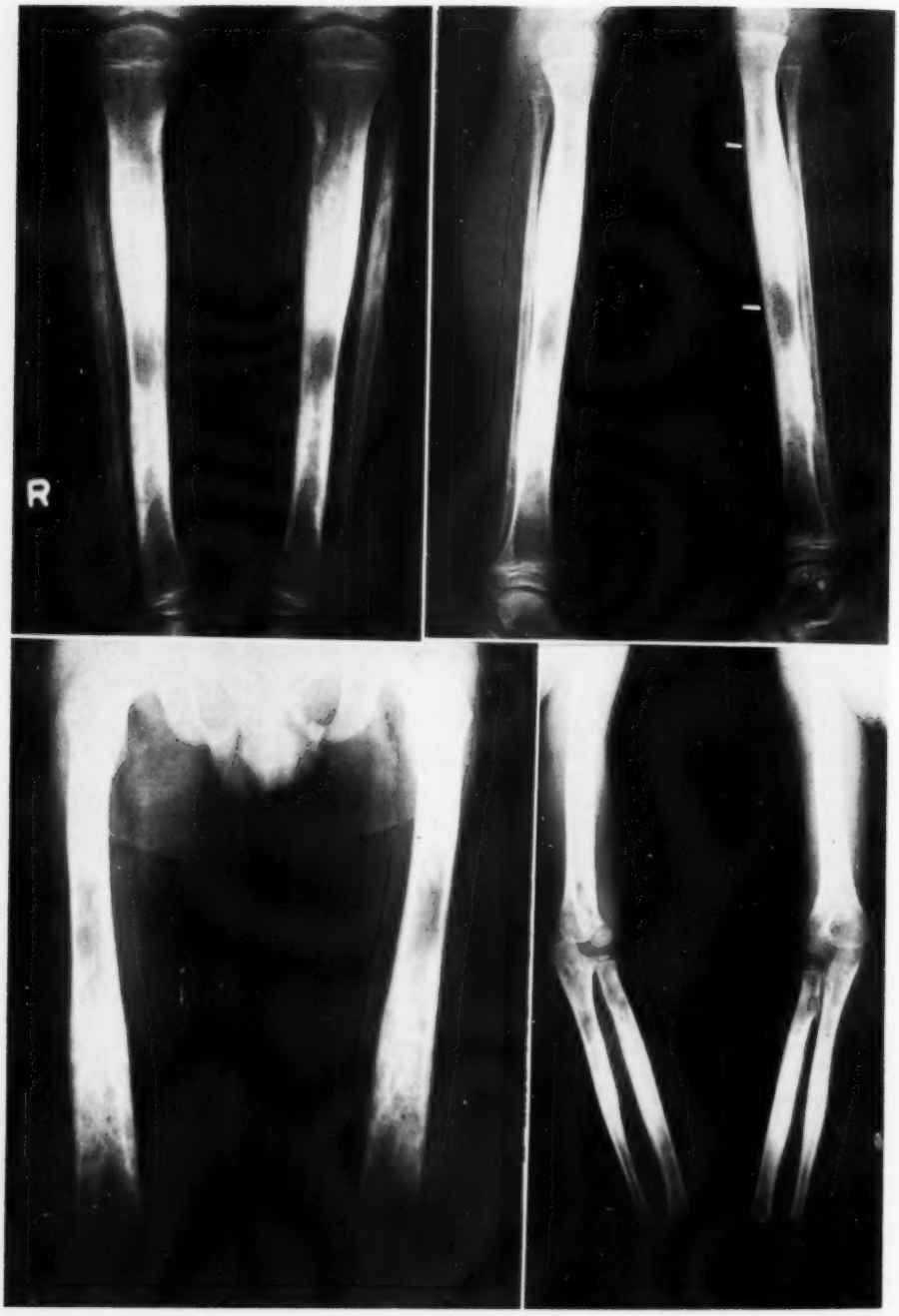

Fig. 2. Long bones of the upper and lower extremities showing fusiform enlargement and sclerosis confined to the diaphyses. The central areas of radiolucency in the mid-portion of each shaft are perhaps in the region of the nutrient vessels. The biopsy specimen extended between the white markers (upper right).

upper and lower extremities were weak. The height was normal, but the weight was only 35 pounds. No joint abnormalities were noted. The deep tendon reflexes appeared slightly hypoactive, more especially in the lower extremities. There was no evidence of sensory impairment. The following laboratory results were obtained:

Serology: Negative (V.D.R.L.).
Blood Count: Hemoglobin, 13.1 gm. per cent; red cells, 4,900,000; white cells, 12,400, with 48 per cent segmented polymorphonuclears, 48 per cent lymphocytes, and 4 per cent eosinophils.
Mean Blood Pressure: 87 mg. Hg.
Blood Chemistry: Calcium, 11.2 mg. per cent; phosphorus, 4.8 mg. per cent; alkaline phosphatase, 10.2 Bodansky units; cholesterol, 266 mg. per cent; blood urea nitrogen, 10 mg. per cent.
Urinalysis: Negative.
Urine Excretion: 17-ketosteroids, 1.7 mg./24 hours; creatinine, 152 mg./24 hours; creatine, 166 mg./24 hours; calcium, 2+ after calcium-free diet. Two-dimensional paper chromatography studies showed no abnormality in urinary excretion of amino acids.
Renal-Function Studies: Glomerular filtration rate, 128 c.c./min. (normal, 80–110); effective renal plasma flow, 936 c.c./min. (normal, 550–700); effective renal blood flow, 1,586 c.c./min. (normal, 1,000–1,200); renal vascular resistance, 0.054 (normal, 0.07); T_{mPAH}, 65 mg./min. (normal, 65–75); flow (urine volume), 0.5 c.c./min. These studies were performed with standard clearance technics. The glomerular filtration rate was measured by the clearance of inulin; renal plasma flow by clearance of sodium paraminohippurate.

Radiographic studies of the skeleton showed a symmetrical fusiform sclerosis involving the diaphysis of each tibia, fibula, femur, humerus, ulna and radius (Fig. 2). The cortex of the affected bones was thickened and the medullary cavity narrowed. Multiple irregular areas of rarefaction were scattered throughout the sclerotic areas. No definite periosteal reaction was present, but the fusiform enlargement of the diaphyses indicated that periosteal new bone formation had been responsible for most of the abnormal configuration. Large localized areas of rarefaction, possibly around nutrient vessels, were present in the mid-portion of each tibia and slightly higher than this in each femur. The involvement was greater in the femora and tibiae. The hands and feet were normal, and there was no evidence of involvement of the pelvis, scapulae, clavicle, ribs, or vertebrae. Questionable slight sclerosis of the floor of the middle fossa was present (Fig. 3).

On May 12, 1955, Dr. Edward T. Smith did a biopsy on the right tibia, extending from the proximal portion of the sclerotic diaphyses into a central area of radiloucency in the mid-portion of the shaft

Fig. 3. Minimal sclerosis of the floor of the middle fossa.

(Fig. 2). The specimen consisted of a narrow piece of bone and adjacent soft tissue measuring 9 cm. in length, 2.5 cm. in thickness, and 1.5 cm. in width. The proximal end of the bone fragment was quite thick (sclerotic) and corresponded to one of the areas of increased density noted on the roentgenogram; the distal end was from an area which radiographically was not involved in the sclerotic process.

Microscopically there was no abnormality of the skin. In the subcutaneous fat, however, there was a single vein, the wall of which was hypertrophied (thickened).

Sections of muscle disclosed loss of some individual muscle fibers in scattered places, with replacement by adipose tissue cells. There were also atrophic muscle fibers with a more eosinophilic staining and sarcolemmal cell nuclei that were slightly pyknotic. The scattering of nuclei throughout the tissue was irregular, suggestive of muscle hyperplasia in some areas. The atrophic fibers also showed hyalinization and a decrease in the prominence of cross striations, with the typical histopathology of Zenker's hyaline degeneration.

In sections displaying periosteum, the outer fiber layer was quite thick, not only over the sclerotic portion of the specimen but equally so over the normal bone. The inner two layers of periosteum (cambium and osteoblastic layers) also showed the same degree of cellularity and thickness over the abnormal and the normal bone.

Arterioles in the periosteum and adventitia around the periosteum had thickened walls, with consequent reduction in the lumens. These arteriolar changes were present in the soft tissues around both the sclerotic and the normal bone. There was some lymphocytic and plasmacytic infiltration around a few small blood vessels in the soft tissue.

The marrow space was reduced in size in the

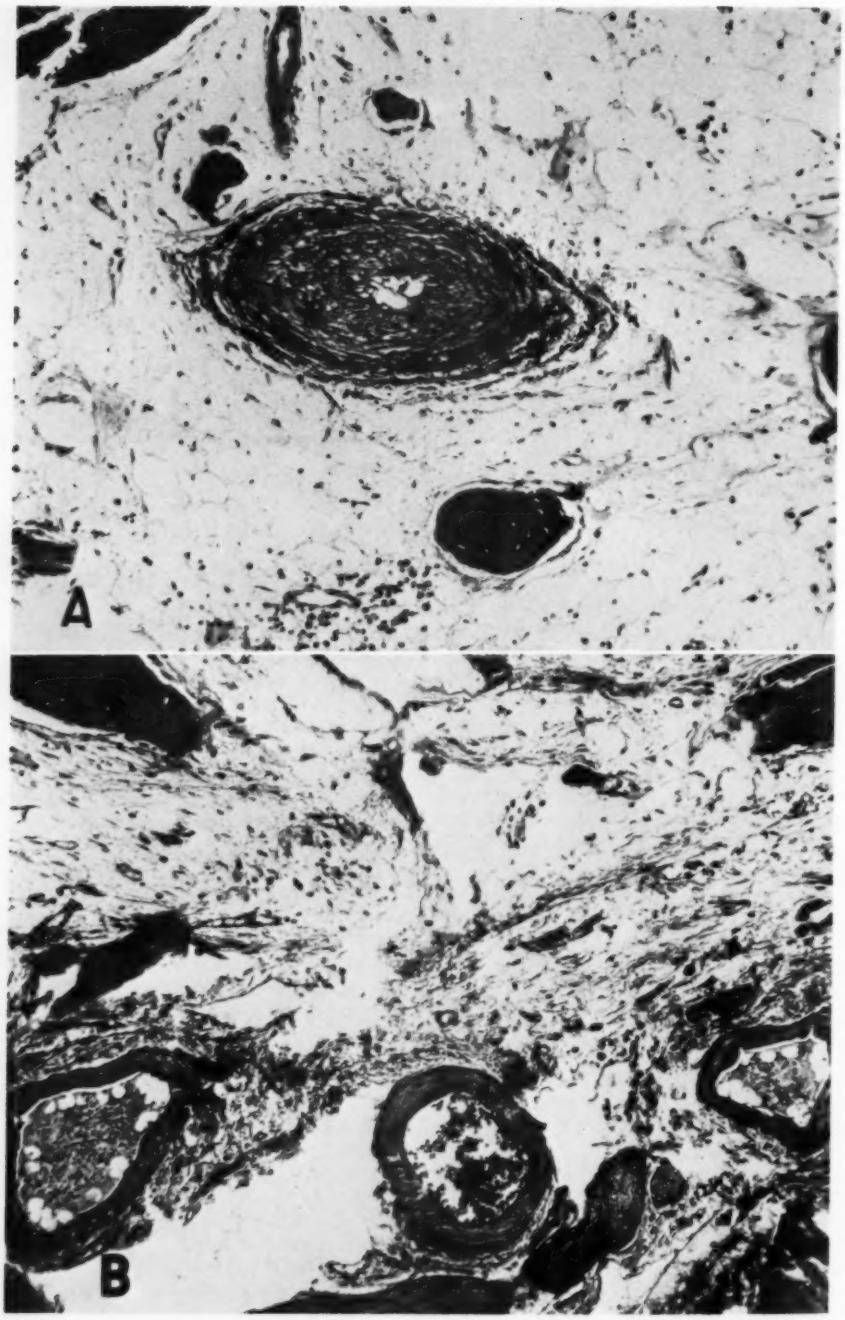

Fig. 4. A. Arteriosclerosis of a vessel in the bone marrow from an area of sclerotic bone. B. Absence of vascular changes in the marrow from the "non-sclerotic" area of biopsy. Hematoxylin and eosin. ×90.

TABLE I: CASES OF ENGELMANN'S DISEASE FROM THE LITERATURE

Author	Sex and Age	Bones Involved	Remarks*
Cockayne (2), 1920	M. 9½ yr.	Frontal bone, base of skull, both femora, both tibiae, one fibula, both humeri	F. H. Negative B. C. Not given
Engelmann (1), 1929	M. 8 yr.	Frontal bone, base of skull, long bones of upper and lower extremities	F. H. None B. C. Unknown
Sear (5), 1948	M. 10 yr.	Frontal bone, base of skull, 1st cervical vertebra, clavicle, scapula, pelvis	F. H. Negative B. C. Slight hypocalcemia; otherwise normal
Neuhauser *et al.* (4), 1948	F. 4 yr. (1941)	Long bones of upper and lower extremities, clavicle	F. H. Negative B. C. Normal
	M. 4 yr. (1942)	Base of skull, long bones of upper and lower extremities	F. H. Negative B. C. Normal
	F. 10 yr.	Long bones of upper and lower extremities, clavicle	F. H. Negative B. C. Normal
	F. 4 yr.	Base of skull, long bones of upper and lower extremities	F. H. Negative B. C. Alkaline phosphatase slightly elevated
Michaelis (6), 1949	F. 24 yr.	Frontal bone, base of skull, long bones of upper and lower extremities	F. H. Brother had gait disturbance
Stronge and McDowell (7), 1950	M. 28 yr.	Frontal and occipital bones, base of skull, long bones of upper and lower extremities	F. H. None B. C. Normal
Bingold (8), 1950	M. 14 yr.	Long bones of lower extremities	F. H. Negative B. C. Normal
Gillespie and Mussey (9), 1951	F. 33 mo.	Base of skull, long bones of upper and lower extremities, clavicle	F. H. Negative B. C. Normal
Gulledge and White (10), 1951	M. 9 yr.	Petrous portion of each temporal bone, long bones of upper and lower extremities	F. H. Negative B. C. Normal
Fairbank (11), 1951	M. 8 yr.	Both femora	F. H. Negative B. C. Normal
Lavine and Koven (12), 1952	M. 12 yr.	Base of skull, long bones of upper and lower extremities	F. H. Negative B. C. Normal
Jammes *et al.* (13), 1953	M. 22 yr.	Base of skull, long bones of upper and lower extremities	F. H. Questionable similar abnormality in father, brother, sister B. C. Normal
Anderson (14), 1953	F. 34 yr.	Frontal bone and base of skull, long bones of upper and lower extremities	F. H. Not mentioned B. C. Not given

* F. H., Familial history. B. C., Blood chemistry.

sclerotic portion of the biopsy specimen, and hematopoiesis was replaced by a myxoid fibro-fatty connective tissue. Hematopoiesis was normal, however, in the uninvolved segments of bone.

In the sclerotic area, the outer part of the cortex was composed of a thin layer of immature bone, beneath which was a considerable quantity of mature laminated bone. Sections from the distal or "normal" segment of the specimen showed a similar but thicker layer of immature bone in the outer portion of the cortex, with a thinner inner zone of mature laminated bone. Osteoblasts were more numerous in the sclerotic portion of the specimen, and in cross sections the haversian canals were generally narrower than normal.

Sections of bone marrow disclosed only a few blood vessels. However, arterioles in the marrow from the sclerotic portion had thick walls and narrow lumens (Fig. 4A), whereas the vessels from the normal portion of the specimen were more numerous and thin-walled (Fig. 4B).

While no blood vessels of any appreciable size were found in the muscle, there were sclerotic changes in the vessels of the subcutaneous tissue.

Although a great variety of conditions will produce hyperostosis of bone, the radiographic and clinical features of Engelmann's disease are typical. The previously reported cases are listed in Table I. The etiology is entirely obscure. Attempts to incriminate an inflammatory process have been unsuccessful, and cultures taken at the time of biopsy in one case (Lavine, 12) were reported as sterile. Serologic studies have been consistently negative. There have been no reports of fever,

Fig. 5. Periosteal reaction and sclerotic regeneration of the cortex six weeks following biopsy.

leukocytosis, or increased sedimentation rate, and the laboratory studies performed have provided no clue to the cause. Excessive ingestion of vitamins A and D, fluorine, or calcium salts have no relationship to the disease and, in contrast to many developmental bone diseases, hereditary factors have been conspicuously absent in most of the reported cases, though in Jammes' case (13) there were bone changes in the patient's brother and sister, as well as a suggestive familial history in the father. Whatever the cause may be, the disease is not limited to the osseous system, since the skeletal muscles are underdeveloped and seemingly account for the ease of fatigability and the characteristic "waddling gait."

ROENTGEN FEATURES

Although the condition may be suspected from the clinical pattern, the roentgen features are diagnostic. The diaphyseal portions of the long bones of the extremities (with the exception of those bones making up the hand) show fusiform enlargement. The normal trabecular pattern is replaced by dense sclerotic bone. The cortex is thickened both from without and from within, and irregular mottled areas of rarefaction may be seen within the sclerotic shafts. In our patient, as well as in Engelmann's original case and at least one of Neuhauser's cases, there was rarefaction in the region of the vascular foramen. Caffey (15) has suggested that this represents absence of the sclerotic process in the region of the nutrient foramen. As the patient grows older, the lesion progresses both proximally and distally, with alteration of the previous normal bone.

In the reported cases the metaphyses and epiphyses have not been involved, except in Anderson's case, in which there appeared to be some involvement of the head of the femur. The soft tissues, including muscles and subcutaneous fat, are sparse.

Films of the right tibia of our patient obtained six weeks following biopsy showed a moderate amount of periosteal new bone formation paralleling the anterior surface of the diaphysis. The periosteal new bone extended proximally over the metaphysis and was smooth and sharply delineated, whereas over the sclerotic area, the newly formed bone was irregular (Fig. 5). Whether this represents a significant difference in the ability of the periosteal cellular elements to react to injury or is simply a reflection of the degree of trauma in the two areas cannot be definitely stated. However, the large defect created by the biopsy was nearly completely replaced in only six weeks by dense bone, indicating that the periosteal reaction in these cases occurs rapidly.

PATHOLOGY

Biopsies have been reported in 8 of the previously reported cases (4, 5, 7, 8, 10, 12).

Two of these were considered as showing essentially normal bone (5, 7). The others invariably revealed increased thickness of the cortical bone and hypertrophy of trabeculae. Periosteal thickening was a frequently reported finding and fibrotic changes of the marrow were described by two authors (4, 12). Neuhauser's cases showed thickening of the periosteum, beneath which was evidence of marked osteoblastic and osteoclastic activity. A later biopsy taken from a different bone of one of these patients revealed an apparent alteration of compact bone to a cancellous type. Biopsy in 2 of Neuhauser's cases showed varying degrees of medial and intimal proliferation of the vessels and obliteration of the lumens of some. This was considered to be a secondary change "indicative of the chronicity of the disease" rather than an etiological factor.

The outstanding pathologic features of the biopsy tissues in our case were muscle atrophy and sclerosis of bone associated with thickening of the walls (predominantly media) and reduction in the size of the lumens of the arterioles of the periosteum, bone marrow, and subcutaneous tissue.

DISCUSSION

Although Engelmann's disease is a rare condition, it is easily recognized if one is aware of its existence. The muscular weakness and "waddling gait" are suggestive clinical signs, and the radiographic findings provide conclusive proof. The most perplexing enigma is the etiology of the disease. In view of the fact that decreased vascularity of bone is associated with increased density, whereas decreased vascularity of muscle is associated with atrophy and necrosis, it is possible that the tissue variations in Engelmann's disease are the simultaneous consequence of a reduced blood flow to these tissues. The presence of vascular changes and luminal narrowing of many of the vessels, as noted in the biopsy specimen from our patient, tend to support this assumption. Similar changes were reported by Neuhauser but were considered to be secondary rather than representative of a primary vascular disease.

Although the vascular changes described in this case may be non-specific, the possibility that they are of significance etiologically should be considered (16). In support of this, is the work of Coolbaugh (17), who reported changes in the strength and density of the dog's femur following interference with its blood supply. Accurate density determinations in grams per cubic centimeter were obtained by use of a radioactive densitometer. On this basis it was found that, following an initial (one to four days) decrease, the density of the bone was definitely increased, exceeding even that of normal bone. This work suggests a causal relationship between Engelmann's disease and bone anoxia secondary to vascular changes. In addition, Thiersch (18) obtained skeletal lesions similar to those of Engelmann's disease by injecting one-day-old chicks intravenously with human myeloid leukemic material. Although there has been no evidence of leukemia in any of the reported cases, the possibility of emboli of the injected material interfering with the blood supply of the experimental animals may perhaps explain Thiersch's results.

A peculiar characteristic of the disease is the confinement of the sclerotic process to the diaphyses, without extension into the corresponding metaphyses and epiphyses. This perhaps can be explained on a vascular hypothesis when one considers the difference in vascularization of the diaphyses and metaphyses. The distal portions of the long bones receive a rich network of vessels from the adjacent periarticular arterial plexus. The metaphysis is thereby furnished with a more adequate blood supply than the corresponding diaphysis (19). One would therefore expect the diaphyses to be more severely affected if the disease is on a vascular basis. Whether or not the rarefactions noted within the sclerotic diaphyses of our patient are due to the proximity

of the nutrient foramen, as suggested by Caffey, is not definitely known but is a possibility worthy of consideration.

An argument against the disease being the result of vascular obliteration is found in the renal function studies of our patient, the renal vascular resistance being low. Although this indicates that obliterative vascular disease is not present in the kidney, it does not negate the idea of the bone changes being the result of vascular occlusion. The increased filtration rate and plasma flow are probably a reflection of the reduction in the patient's calculated surface area incident to muscle atrophy and weight loss from his disease.

Osteopetrosis and melorheostosis are other bone diseases which show sclerosis, but the distribution is unlike that seen in Engelmann's disease and the clinical findings are also completely different. Although Lavine has suggested that these lesions may have a similar etiology and represent different stages of the same process, there is no substantial proof for this assumption.

SUMMARY

Engelmann's disease (progressive diaphyseal dysplasia) is a rare disorder of bone characterized by weakness and underdevelopment of the muscles of the extremities and fusiform sclerosis of the diaphyses of the long bones. The previously reported cases are reviewed and an additional case is submitted. The presence of thickening of the vessel walls in the biopsy specimen in this latter case suggests that the disease may be on a vascular basis.

NOTE: Acknowledgment is made to Mr. R. M. Christopher, of Baylor University College of Medicine, and Mr. Gene Davis, of Methodist Hospital, Houston, Texas, for the photographic work.

REFERENCES

1. ENGELMANN, G.: Ein Fall von Osteopathia Hyperostotica (Sclerotisans) Multiplex Infantilis. Fortschr. a. d. Geb. d. Röntgenstrahlen **39:** 1101–1106, June 1929.

2. COCKAYNE, E. A.: Proc. Roy. Soc. Med. (Section for the Studies of Disease in Children). **13:** 132, 1920.

3. RILEY, C. M., AND SHWACHMAN, H.: Unusual Osseous Disease with Neurologic Changes. Report of 2 Cases. Am. J. Dis. Child. **66:** 150–154, August 1943.

4. NEUHAUSER, E. B. D., SHWACHMAN, H., WITTENBORG, M., AND COHEN, J.: Progressive Diaphyseal Dysplasia. Radiology **51:** 11–22, July 1948.

5. SEAR, H. R.: Engelmann's Disease. Osteopathia Hyperostotica Sclerotisans Multiplex Infantilis; Report of a Case. Brit. J. Radiol. **21:** 236–241, May 1948.

6. MICHAELIS, L. S.: Engelmann's Disease. Proc. Roy. Soc. Med. **42:** 271–273, April 1949.

7. STRONGE, R. F., AND MCDOWELL, H. B.: A Case of Engelmann's Disease; Progressive Diaphyseal Dysplasia. J. Bone & Joint Surg. **32-B:** 38–39, February 1950.

8. BINGOLD, A. C.: Engelmann's Disease: Osteopathia Hyperostotica (Sclerotisans) Multiplex Infantilis. Brit. J. Surg. **37:** 266–274, January 1950.

9. GILLESPIE, J. B., AND MUSSBY, R. D.: Progressive Diaphyseal Dysplasia (Engelmann's Disease). J. Pediat. **38:** 55–59, January 1951.

10. GULLEDGE, W. H., AND WHITE, J. W.: Engelmann's Disease (Progressive Diaphyseal Hyperostosis). Report of a Case. J. Bone & Joint Surg. **33-A:** 793–797, July 1951.

11. FAIRBANK, T.: An Atlas of General Affections of the Skeleton. Edinburgh, E. & S. Livingstone, 1951.

12. LAVINE, L. S., AND KOVEN, M. T.: Engelmann's Disease (Progressive Diaphyseal Dysplasia). J. Pediat. **40:** 235–239, February 1952.

13. JAMMES, A., SERNY, K., PROUZET, J., AND DUCLOS, G.: Maladie d'Engelmann: osteopathie hyperostante et sclerosante infantile multiple; à propos d'une nouvelle observation. Rev. du rhum. (Paris) **20:** 406–414, May 1953.

14. ANDERSON, F. G.: Engelmann's Disease. Brit. J. Radiol. **26:** 603–607, November 1953.

15. CAFFEY, J.: Pediatric X-Ray Diagnosis. A Textbook for Students and Practitioners of Pediatrics, Surgery, and Radiology. Chicago, The Yearbook Publishers, Inc., 2d ed., 1950.

16. DAESCHNER, W. (Pediatric Department, Baylor University College of Medicine, Houston, Texas): Personal communication.

17. COOLBAUGH, C. C.: Effects of Reduced Blood Supply on Bone. Am. J. Physiol. **169:** 26–33, April 1952.

18. THIERSCH, J. B.: Contribution to the Radiology and Pathology of Transmissible Avian Osteopetrosis—Lymphomatosis. Radiology **51:** 100–110, July 1948.

19. CLARK, W. E. LE GROS: The Tissues of the Body: An Introduction to the Study of Anatomy. New York and London, Oxford University Press, 3d ed., 1952.

SUMARIO

Displasia Diafisaria Progresiva (Enfermedad de Engelmann)

La enfermedad de Engelmann (displasia diafisaria progresiva) es un trastorno raro de los huesos, caracterizado por debilidad y desarrollo incompleto de los músculos de los miembros y esclerosis fusiforme de las diáfisis de los huesos largos. Repásanse los casos y comunicados, agregándose uno nuevo. La existencia de espesamiento de las paredes vasculares en el ejemplar obtenido con la biopsia en este último caso sugiere que la dolencia tal vez reconozca base vascular.

A New Sign in the Diagnosis of Cardiac Aneurysm and Myocardial Infarction

(Respiratory Phenomenon; Effort Test; Paradoxical Expansion of the Heart)[1]

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Istanbul, Turkey

ANY ONE OF A number of conditions—tumors and cysts of the heart and pericardium, aneurysms of the sinus of Valsalva, mediastinal tumors, dilatation of the left ventricle, and encroachment of the right ventricle upon the left ventricular border—will produce a radiologic image similar to that of cardiac aneurysm. Differentiation of these conditions may thus be extremely difficult. Even kymographic studies may fail to discriminate between them. Yet a correct diagnosis is important for arriving at a prognosis and determining the indications for treatment.

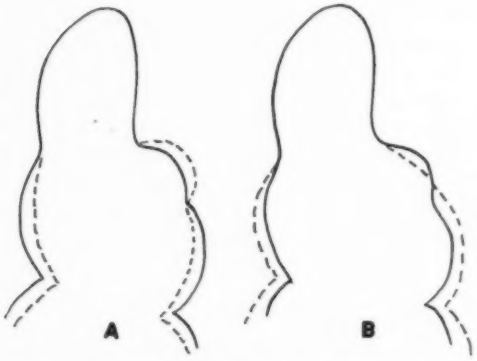

Fig. 1. Respiratory phenomenon in cardiac aneurysm. A. In forced inspiration. B. In forced expiration.

Respiratory Phenomenon in Cardiac Aneurysm: The method to be described here for the diagnosis of cardiac aneurysm consists in fluoroscopic or radiographic examination of the heart alternately in forced inspiration and expiration. During forced inspiration the amount of blood entering the heart from the systemic and pulmonary circulations is decreased. The lung, overdistended with air, presses upon the heart with the result that the cardiac shadow becomes smaller and the intracardiac pressure is increased. At the same time, a rise in intrapleural negative pressure exerts a sucking effect upon the aneurysmal sac, which, having lost its tonicity, becomes distended and more prominent (Fig. 1A).

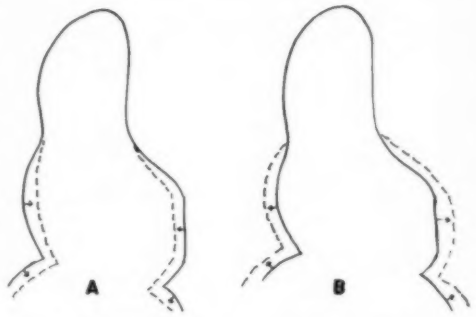

Fig. 2. Respiratory phenomenon in myocardial infarction. A. In forced inspiration. B. In forced expiration.

During forced expiration these conditions are reversed. The lung retracts because of the outflow of air, a greater amount of blood enters the heart and it becomes larger, while the intracardiac pressure decreases. The aneurysmal sac collapses, disappearing completely, and the left ventricular border loses its convexity and becomes flat (Fig. 1B).

This respiratory phenomenon is indicative of a cardiac aneurysm. In the other conditions mentioned above, the bulging which in routine views may lead to an incorrect diagnosis remains the same in both phases of respiration.

Respiratory Phenomenon in Myocardial Infarction: Pericardial adhesions localized to the left ventricular border simulate myocardial infarction radiologically. Here also a diagnosis may be made by examination in forced inspiration and expiration. In this instance the mechani-

[1] Accepted for publication in July 1955.

cal pressure effect of the distended lung upon the heart is most apparent in the area of infarction, where the myocardium has lost its tonicity. Retraction takes place, and the involved area appears flattened or even depressed. With forced expiration, the line of infarction disappears completely and the normal convexity of

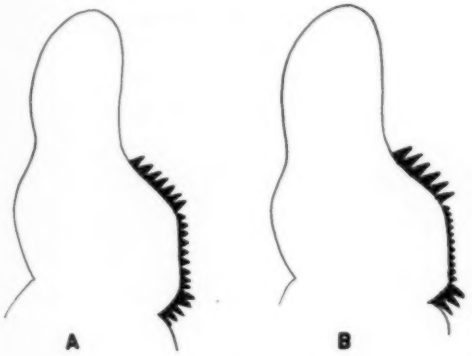

Fig. 3. Effort test in myocardial infarction. A. Before exertion. B. After exertion.

the left ventricular border is restored (Fig. 2). No such change with the respiratory phases is observed in pericardial adhesions.

Effort Test in Myocardial Infarction: In the presence of direct radiological signs myocardial infarction is readily recognized. When, however, clinical and radiologic evidence is minimal, diagnosis becomes difficult. Particularly is this true in cases of myocardial weakness. In these cases a comparison of kymograms obtained before and after slight or moderate effort may be conclusive. Following exertion, the pulsations above and below the area of infarction will be found to be increased in amplitude, while those in the area itself will have become reduced or even have disappeared altogether (Fig. 3).

Paradoxical Respiratory Expansion of the Heart in Total Cardiac Aneurysm: The diagnosis of total aneurysm of the heart is attended by great difficulty. The large

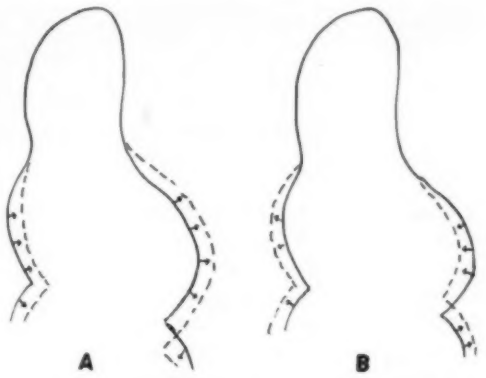

Fig. 4. Paradoxical respiratory expansion of the heart in total cardiac aneurysm. A. In forced inspiration. B. In forced expiration.

heart shadow and decreased contractions over the left ventricular border are suggestive of ventricular enlargement or myocardial weakness. The effects of forced inspiration and expiration in these cases are directly contrary to those on the normal heart. With inspiration there is an outward expansion of the left ventricular border and an increase in heart size attributable to the effect of the heightened negative pleural pressure. Conversely, in expiration there occurs an inward retraction of the left ventricular border, with a reduction of heart size (Fig. 4).

SUMMARY

A method of diagnosis of cardiac aneurysms and myocardial infarction based on roentgenologic examination of the heart in forced inspiration and expiration is presented.

An effort test for myocardial infarction is also suggested, and paradoxical expansion of the heart in total cardiac aneurysm, as demonstrated on forced inspiration and expiration, is described.

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(*Para el sumario en español véase la página 246.*)

Ninety Per Cent Hypaque for Rapid Intravenous Roentgenography

Preliminary Report[1]

NATHANIEL FINBY, M.D., NATHAN POKER, M.D., and JOHN A. EVANS, M.D.

HIGHLY CONCENTRATED iodinated contrast media are needed for rapid intravenous injection in angiocardiography and nephrotomography. The present study documents the use of 90 per cent Hypaque in 50 consecutive patients, with a detailed analysis of reactions and results.

CHEMISTRY AND PHARMACOLOGY

Hypaque is a white crystalline solid which contains 59.87 per cent iodine and is highly water-soluble. Chemically, it is sodium 3,5-diacetamido-2,4,6,-triiodobenzoate, which is related structurally to Urokon (sodium acetrizoate). The acetrizoate formula is the basis for a group of contrast agents which may be of value in radiologic investigation.

Sodium Hypaque has been extensively utilized in 50 per cent solution for intravenous urography and has proved satisfactory for that purpose (1). An attempt to produce a more concentrated solution resulted in the development of 90 per cent Hypaque, which consists of 30 per cent Sodium Hypaque and 60 per cent Methylglucamine Hypaque. This product is not soluble at room temperature and must be warmed for complete solubility and a clear solution. When completely dissolved, it has proved stable in solution for at least three or four hours, but on cooling the liquid tends to become more viscous. Since this latter property interferes with rapid injection, freshly warmed solutions are necessary.

Although Hypaque is utilized as a 90 per cent solution (90 gm. per 100 c.c.), the actual iodine content in the usual 50-c.c. dose is 23.0 gm. Urokon in 70 per cent solution (70 gm. per 100 c.c.) has an iodine content of 23.1 grams in the usual 50-c.c. dose. Thus, although 90 per cent Hypaque is more concentrated, the actual iodine content is not increased.

METHODS AND MATERIAL

Angiocardiography and nephrotomography in the average unanesthetized adult require rapid intravenous injection of 50 c.c. of concentrated contrast material within two seconds. Angiocardiography (2) is usually performed in the upright position and nephrotomography (3) in the supine position.

We have injected 28 patients for angiocardiographic study and 22 patients for nephrotomographic study. Twenty-two of these patients received two injections, usually within a fifteen-minute interval. Thus, there has been a total of 72 injections of 90 per cent Hypaque. Of the 50 patients, 31 were male and 19 female; the youngest was thirteen years and the oldest seventy-six years of age. The dose has varied between 30 and 50 c.c. per injection, depending upon the size and the age of the patient. Four patients received less than 50 c.c. per injection.

RESULTS

The rapid injection of concentrated contrast material for angiocardiography or nephrotomography is frequently associated with symptoms referable to the speed of injection, the excitement of the examination, and the material used. In contrast to routine intravenous urography, a high percentage of reactions is accepted as a part of the examination (4). It is therefore encouraging to find a new contrast material which subjectively and objectively appears to reduce these side-effects.

[1] From the Department of Radiology, The New York Hospital-Cornell Medical Center, New York, N. Y.

It is of interest that 3 of our patients, previously examined angiocardiographically with other media, volunteered the information that 90 per cent Hypaque was "easier to take," "less strong," or "milder." Also, the objective appraisal of the general reaction by experienced observers indicates that 90 per cent Hypaque causes fewer and less severe reactions than other concentrated contrast media.

Since these observations are difficult to analyze, it is worthwhile to catalogue the reactions, as in Table I, where 90 per cent Hypaque is compared with 70 per cent Urokon (4).

It is noteworthy that a significant decrease in nausea, cough, arm pain, vomiting, weakness, urticaria, and thirst was observed with 90 per cent Hypaque. Vertigo occurred in 14 per cent and flush was noted in 90 per cent of the patients. Five mentioned a metallic or acid taste and 1 complained of some transient "tightness" in the chest.

Eight of 10 patients receiving a single injection of 90 per cent Hypaque after transcutaneous insertion of the Robb-Steinberg needle had thrombosis. This complication may be expected in a high percentage of patients when concentrated hypertonic solutions are injected rapidly. Only one instance of significant phlebitis occurred in our 50 patients. This responded quickly to routine measures. Blood pressure remained stable except for slight elevations or depressions. No syncope or severe depression of blood pressure was observed.

Radiographic study showed satisfactory visualization of cardiovascular and pulmonary structures in angiocardiography and of the aorta and kidneys in nephrotomography. Opacification of these structures with 90 per cent Hypaque is comparable to that obtained with 70 per cent Urokon.

TABLE I: COMPARISON OF REACTIONS ASSOCIATED WITH RAPID INTRAVENOUS INJECTION OF 70 PER CENT UROKON AND 90 PER CENT HYPAQUE

Reaction	70% Urokon Sodium (2 injections*	90% Hypaque (2 injections)†	90% Hypaque (all patients)‡
Heat	100	100	96
Flush	68	87	90
Nausea	40	23	24
Headache	32	23	20
Cough	44	9	8
Vertigo		14	8
Arm pain	20	0	6
Vomiting	12	5	4
Weakness	80	0	2
Urticaria	20	5	4
Thirst	72	0	2
Wheezing	4	0	0
Palpitations	24	0	0

* Twenty-five patients, each receiving 2 injections of 50 c.c. 70 per cent Urokon (4).

† Twenty-two patients, each receiving 2 injections of 50 c.c. 90 per cent Hypaque.

‡ Fifty patients receiving one or two injections of 90 per cent Hypaque.

SUMMARY

Experience with a new concentrated intravenous contrast material, 90 per cent Hypaque, for rapid injection in angiocardiography and nephrotomography indicates that good contrast visualization is obtained with a decreased number of side reactions. This new material was well tolerated in 50 patients without any serious complications.

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REFERENCES

1. LOWMAN, R. M., SHAPIRO, H., LIN, A., DAVIS, L., KORN, F. E., AND NEWMAN, H. R.: Preliminary Clinical Evaluation of Hypaque in Excretory Urography. Surg., Gynec. & Obst. **101**: 1–8, July 1955.
2. DOTTER, C. T., AND STEINBERG, I.: Angiocardiography. Annals of Roentgenology, Vol. 20. New York, Paul B. Hoeber, Inc., 1951.
3. EVANS, J. A., MONTEITH, J. C., AND DUBILIER, W., JR.: Nephrotomography. Radiology **64**: 655–663, May 1955.
4. DOTTER, C. T., WETCHLER, M. S., AND STEINBERG, I.: Contrast Substances for Angiocardiography. Study of Side Effects. Radiology **60**: 691–698, May 1953.

(Para el sumario en español véase la página siguiente.)

SUMARIO

Hypaque de 90 per Ciento, para la Roentgenografía Intravenosa Rápida: Informe Preliminar

El empleo de una nueva substancia intravenosa concentrada de contraste, el Hypaque al 90 por ciento, para rápida inyección en la angiocardiografía y la nefrotomografía, indica que obtiene buena visualización de contraste con un número menor de reacciones colaterales. Esta nueva substancia fué bien tolerada por 50 enfermos sin ninguna complicación grave.

El estudio radiográfico reveló visualización satisfactoria de los órganos cardiovasculares y pulmonares en la angiocardiografía y de la aorta y los riñones en la nefrotomografía La opacidad obtenida en estos órganos fué comparable a la del Urokón al 70 por ciento.

SUMARIO

Nuevo Signo en el Diagnóstico del Aneurisma Cardíaco y del Infarto Miocardíaco (Fenómeno Respiratorio; Prueba del Esfuerzo; Expansión Paradójica del Corazón)

(Página 242)

Descríbese un método de diagnóstico para los aneurismas cardíacos y los infartos miocardíacos, basado en el examen del corazón durante la aspiración y la espiración forzadas. En la aspiración forzada, el saco del aneurisma se distiende y proyecta, mientras que en la espiración se aplasta, dejando un borde aplanado en el ventrículo izquierdo. En el infarto miocardíaco, la aspiración forzada se acompaña de retracción de la zona infartada, mientras que en la espiración el borde del ventrículo izquierdo recobra su convexidad normal.

Se sugiere además una prueba del esfuerzo para el infarto miocardíaco y se describe la expansión paradójica del corazón en el aneurisma cardíaco, según se observa en la aspiración y la espiración forzadas.

Intravenous Cholangiography in the Presence of Jaundice[1]

DAVID ROSENBLUM, M.D., and SOLOMON SCHWARTZ, M.D.

CHOLOGRAFIN 20 per cent (sodium N,N′-adipylbis (3-amino-2,4,6,-triiodo) benzoate, Squibb) is of inestimable value in demonstrating the common duct of the cholecystectomized patient. That it is useful also in the presence of jaundice is not so well known. Published accounts of visualization of the ducts of jaundiced patients are few in number. Hastings-James and Glazebrook (1) report successful visualization in 1 of 2 cases. The degree of jaundice is not stated. Aldridge (2) was successful in 6 of 15 cases. His criteria for selection of patients were perhaps less rigid than those adopted by us, in that he included in his series patients who had been jaundiced within one week of the examination.

Because the icterus index appears an unreliable criterion, we have used a serum bilirubin of 1.0 and above (normal in our laboratory 0.8) as indicative of jaundice.

To date, we have attempted intravenous cholangiography with Cholografin in 26 jaundiced patients and have succeeded in visualizing the common duct in 5 (Figs. 1–5), or 19 per cent. Actually, in 1 case, the examination was not completed because of severe nausea and vomiting. If this case is discounted, the percentage of successful visualization rises to 20 per cent. In 2 cases the common duct was not visualized initially but was demonstrated later. In the first of these, failure occurred with an icterus index of 15 and a serum bilirubin of 1.8. Successful cholangiography was performed when these values had fallen to 10 and 0.9, respectively. In the second case, initial values were 16 and 1.8 but had decreased to 8 and 0.8 several days after cholangiography. No values were available for the date on which the examination was performed. Neither of these cases is included as a successful visualization in the presence of jaundice.

Fig. 1. Bilirubin 1.4. Icterus index 9. Arrow points to stone in cystic duct. Slight narrowing of terminal portion of common duct. Marked distention of hepatic and common ducts. Contrast material in duodenum.

The highest icterus index at the time of visualization was 22 and the highest serum bilirubin 3.3. Whenever serial serum studies are available, they appear to indicate that jaundice was on the wane at the time of visualization of the common duct. The highest values given occurred in a case in which, five days later, the icterus index and serum bilirubin had fallen to 8 and 1.3, respectively. Average values at the time of visualization were 12 for the icterus index and 1.7 for serum bilirubin.

Serum bilirubin values are available in 20 of the 21 failures. At the time of cholangiography in these cases, jaundice was waning in 9, static in 5, and increasing in

[1] From the Department of Radiology, The Jewish Hospital of Brooklyn. Accepted for publication in July 1955.

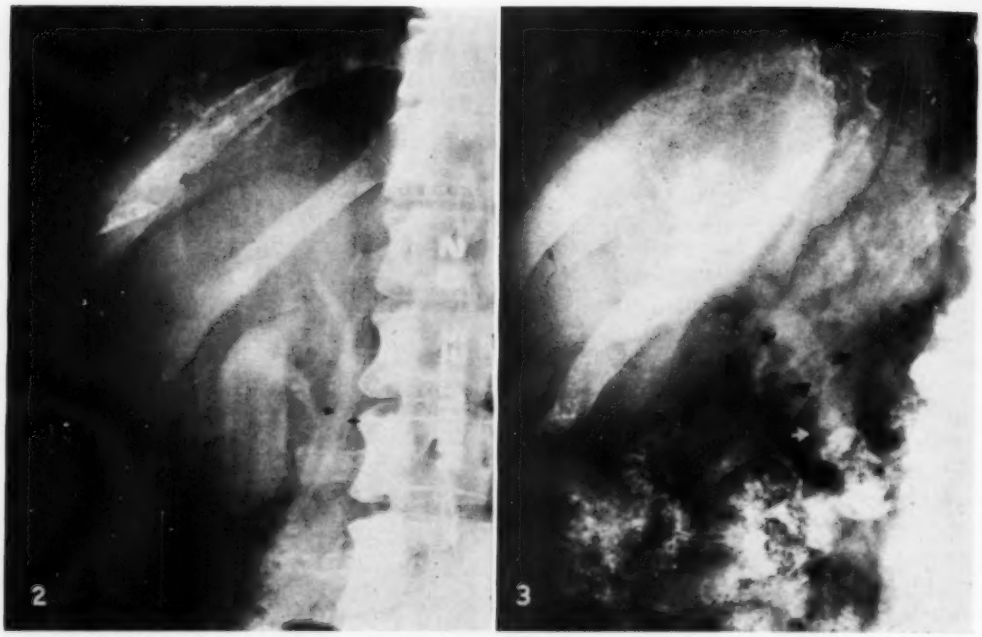

Fig. 2. Bilirubin 3.3. Icterus index 22. Arrows point to normal common duct. Gallbladder visualized. Clinical diagnosis was Thorazine reaction.

Fig. 3. Bilirubin 1.2. Icterus index 14. White arrow points to stone in distal end of faintly visualized common duct.

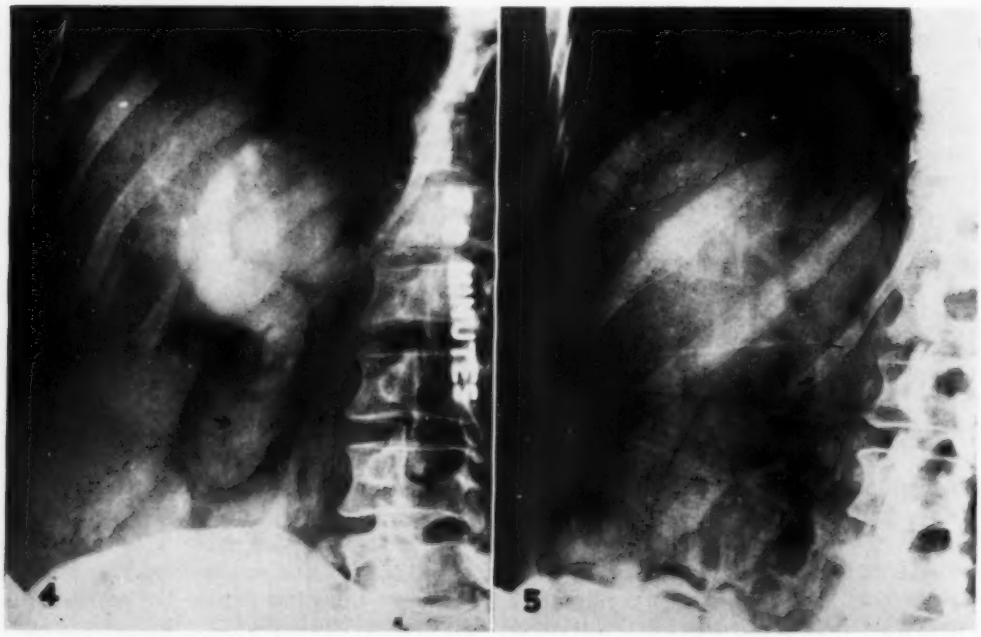

Fig. 4. Bilirubin 1.1. Icterus index 7. Arrow points to stone in distal end of markedly dilated common duct.

Fig. 5. Bilirubin 1.5. Icterus index 8. Arrows point to faintly visualized but normal common duct. (This patient had a cholecystectomy twenty-one years previously; note the common duct of normal size.) The clinical diagnosis was biliary cirrhosis.

6. In only 1 case with waning jaundice were the values below the averages given for adequate visualization. In this instance success was subsequently obtained, but the case was counted among the failures because exact values at the time of examination were not known. In all other failures, serum values at the time of examination were higher than the averages for successful visualization.

There seem thus to be two prerequisites to successful visualization of the common duct: (*a*) waning jaundice and (*b*) icterus index and serum bilirubin values within certain limits. It may be that the average values of 12 for the icterus index and 1.7 for serum bilirubin will be pushed upward by the use of concentrated Cholografin (40 per cent) and morphine. These agents may also increase the percentage of successful visualizations. Aldridge, using pethidine (Demerol), was able to demonstrate the common duct with an average serum bilirubin of 3.2. Two factors may explain this high value. One is the fact that the figures given may have been obtained as long as a week prior to cholangiography. The other is the use of a spasmodic. We have tried morphine in 2 jaundiced patients, obtaining visualization in 1. This patient had a serum bilirubin of 2.5 and icterus index of 25. Jaundice, at the time of examination, was waning. In the unsuccessful case, bilirubin was 8.7, the icterus index was 48, and jaundice was increasing. Neither case is included in the 26 reported above. Concentrated cholografin was not available to us at the time of the study reported here.

Duration of jaundice, degree of liver damage, and type of jaundice are factors yet to be studied.

SUMMARY

Intravenous cholangiography with Cholografin was successful in 5 of 26 jaundiced patients. The relationship of the results to the icterus index and serum bilirubin values is reported. Values not exceeding 12 and 1.7, respectively, especially when jaundice is waning, would appear to justify efforts at duct demonstration.

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REFERENCES

1. HASTINGS-JAMES, R., AND GLAZEBROOK, A. J.: Cholografin. Canad. M. A. J. **72**: 561–565, April 15, 1955.

2. ALDRIDGE, N. H.: Rapid Examination of the Biliary Tract. A New Technique with Biligrafin. J. Fac. Radiologists **6**: 243–253, April 1955.

SUMARIO

La Colangiografía Intravenosa en Presencia de Ictericia

La colangiografía intravenosa con Colografín obtuvo éxito en 5 de 26 ictéricos. El índice ictérico más alto en el momento de la visualización fué de 22 unidades y la cantidad más alta de bilirrubina sérica representó 3.3 mg. Siempre que se cuenta con estudios séricos en serie, parecen indicar descenso de la ictericia al visualizar el colédoco. En el momento de la visualización, los valores medios eran de 12 unidades para el índice ictérico y de 1.7 mg. para la bilirrubina sérica. Parece, pues, que precisan dos requisitos para la visualización del colédoco: (*a*) ictericia en descenso y (*b*) valores del índice ictérico y de la bilirrubina sérica dentro de ciertos límites.

Valores que no excedan los indicados, sobre todo si la ictericia va declinando, parecen justificar la iniciación de esfuerzos encaminados a descubrir los conductos.

On the Statistical Nature of Mortality, with Especial Reference to Chronic Radiation Mortality[1]

GEORGE A. SACHER

AN IMPORTANT problem in radiation biology today is that of estimating the consequences, in illness and mortality, for human populations exposed to ionizing radiations in arbitrary amount and temporal distribution. Since an experimental determination is precluded, we must rely principally on information obtained from animals. The problem then arises of making valid inferences about effects on man in terms of laboratory experience.[2] Such inference is possible in principle only in so far as there are common terms between the lower mammals and man, arising from their homologies with respect to physiologic constitution. It is presumed that homologous systems of different species are alike in mechanism, that they differ in the numerical values of their parameters, and that these parameters can be estimated for the species concerned.

Projection from animals to man can then be carried out as indicated schematically in Figure 1. This diagram brings out the importance for interspecies prediction of the relation between physiologic effects and lethality within species. The present paper is devoted to establishing the nature of this relation. Equally important is the problem of understanding and quantitatively describing physiologic injury. This latter aspect will not be discussed here.

STATISTICAL NATURE OF THE DEATH PROCESS

It is an intuitive judgment on the basis of clinical and laboratory experience that the occurrence or non-occurrence of death in a given interval cannot be predicted with certainty in the individual case, however precisely the conditions be known or controlled. This judgment has a counterpart in the fact that the future behavior of a directly observed physiologic process cannot be predicted with certainty, even with extensive information about its past behavior.

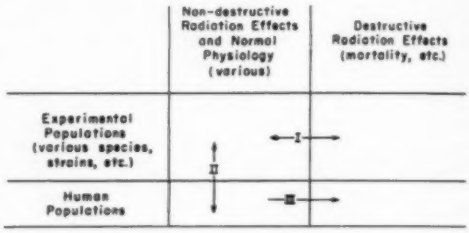

Fig. 1. Diagrammatic presentation of the kinds of observations and relations required to permit interspecies prediction of a response (mortality) that can be studied directly in one or more experimental species, but not in man. Mortality in experimental species must first be understood in terms of their physiology (relations of type I). Quantitative relationships between human and animal physiology must also be established (type II relations). A prediction of human mortality (type III relations) is then possible in principle, based on relationships of types I and II. These relations can be verified by experiment. The amount of information that would be needed to carry out such a program is certainly much greater than the amount available at present.

Considerations such as these lead to the hypothesis that the unpredictability of mortality is a consequence of the uncertainty that is inherent in the dynamics of physiologic function. According to this hypothesis, the occurrence within an organism of a failure of function leading to death is the result of a fluctuation of the physiologic state of the organism, of such magnitude as to exceed the limits within which

[1] From the Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill. Presented at the Forty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 13–16, 1955. Work performed under the auspices of the U. S. Atomic Energy Commission.

[2] The information gained from radiation therapy and from the Japanese atomic weapon casualties is of great value for the prediction of effects on man. We must face the possibility, however, that this information will not be sufficient by itself for a solution of the prediction problem. The safest program is to develop a methodology of prediction on the presumption that such human experience does not exist.

homeostatic regulation can occur.[3] The mathematical problem becomes one of determining how frequently such extreme fluctuations occur as a function of the homeostatic parameters of the organism or population. This is equivalent to finding a new kind of quantitative measure for the homeostatic capacities of organisms.

As a starting point for the development of this theory, we shall examine the hypothetical case of a homogeneous population in which all members are indistinguishable one from another. Such a population is defined by the specification that the physiologic processes of all members have the same mean values and the same magnitudes and rates of fluctuation. Hence the probability that, in a time interval, t, a fluctuation will occur to or beyond a limit value, L, is the same for every individual. In n samples from this population, let the mean physiologic states be displaced from the pre-existing common mean, m, to a series of different values, $m_1 . . m_i . . m_n$, for a time t. We may consider this to have been done by applying "dosages" $D_1 . . D_i . . D_n$. Then the probabilities, $p_1 . . p_i . . p_n$, of fluctuation beyond L will be different for each sample group. This probability is, by hypothesis, the probability of death, so that the plot of p_i *vs.* D_i is a dosage-survival curve. It can be shown that, if the fluctuation process has the characteristics of actual physiologic fluctuation processes, then the survival curve so determined has the sigmoid form and other characteristics of empirically determined survival curves. *Yet this survival curve would have been generated from a population in which there was no pre-existing distribution of radiosensitivities.*

In actual populations, differences between individuals are always present to some degree. This can be taken into account by introducing the frequency distributions of parameters that vary in the population. To this extent the present theory has something in common with one widely accepted, which holds that the genesis of the mammalian dosage-survival curve is *entirely* due to the distribution of a sensitivity parameter in the population. A flaw of the latter theory is that it does not lead to an understanding of the relation of mortality to the dynamics of physiologic function. Such understanding is a necessary condition for the development of a quantitative physiology of death, but it should also have significance for the study of physiologic regulation in general.[4]

DISCUSSION OF AN EXPLICIT MODEL FOR A STOCHASTIC MORTALITY PROCESS

Stochastic processes (1) fall into four major classes, depending on whether the variable moves continuously or by discrete steps, and whether the process is stationary (time-independent) or non-stationary. Instances of all four types may be found in biology. For example, the highly de-

[3] The term, *physiologic state*, as employed herein may be defined approximately as follows. An organism is considered for the present purpose to be a physical system which can be described as of a given moment in time by determining the numerical values of all metabolite concentrations, cell population sizes, etc., at that moment. The number of quantities to be assigned for an exact description would be unmanageably large. It is assumed that a description that has a tolerable error can be given by specifying a considerably smaller number, perhaps of the order of tens, of properly chosen variables. This set of numbers is called the *physiologic state*. The state of an individual cannot, in fact, be specified moment by moment. The operationally attainable description is in terms of the average values, frequency distributions, intercorrelations, and lag correlations of the variables. This description in terms of the expected values of the variables is called the *mean physiologic state*. The analysis of mortality given here is based on the presumption that the mean physiologic state comprises all that can be said about the population. Additional information may be accessible in laboratory situations, and, if so, it can also be used in prediction. Finally it may be remarked that the concept of state enunciated above is applicable only to the vegetative aspects of behavior, and there only in approximation.

[4] The literature on the mathematical analysis of mortality is too extensive for adequate review here. Thus, the assertion that the developments presented here are not foreshadowed in any previous mathematical treatment must remain undocumented for the present. The fundamental distinction is that previous treatments sought to develop equations relating mortality to *external* physical variables such as chronological age (in the case of life tables) or dose of a toxic agent (in the case of survival curves), whereas the procedure here is the first to account for mortality in terms of the statistical nature of physiologic processes. A relation of mortality to external variables requires a further specification of the dependence of the physiologic process on dose and time (or age). These two steps are so profoundly different in kind that they cannot be reduced to one, as in previous attempts.

veloped "target" theories of radiation effects on micro-organisms are instances of discrete, non-stationary random processes. In this paper only continuous stationary Gaussian (2) processes are considered, because homeostatically regulated variables appear to have fluctuation processes of this type. There is also a non-stationary stochastic component in the maturation and aging of all biologic processes, but this topic needs more extensive consideration than can be given here.

The model I shall consider is a very simple one. It leads, however, to a functional relation between mean physiologic state and probability of mortality which is the same as the relation obtained from more complicated and veridical models. A high degree of mathematical elaboration is of little use in the present primitive state of the experimental aspects of the subject.

A random force function, $f(t)$, arising from environmental and internal sources, causes displacements of a variable, x, from its average (stationary) value, m. The random function has a time-average value of zero, and its moment-to-moment variation is of the incoherent kind that engineers are accustomed to refer to as "white noise." The displacement μ ($\mu = x - m$) is considered to obey the stochastic differential equation

$$\frac{d\mu}{dt} + g\mu = f(t) \tag{1}$$

where g is a constant with dimensions t^{-1}. It can be shown that the distribution function describing the behavior of a system for which Equation 1 is the equation of motion may be obtained from the solution, with appropriate boundary conditions, of the partial differential equation

$$\frac{\delta P}{\delta t} = g\frac{\delta}{\delta \mu}(\mu P) + D\frac{\delta^2 P}{\delta \mu^2} \tag{2}$$

which is a special form of the Fokker-Planck equation (2). Here P represents the conditional probability, $P(\mu_0 \mid \mu,\ t)$, that a particular value, μ, will be observed at time t, given that the system had the value μ_0 at time zero. The coefficient D is a dispersion parameter of the random force function.

The steps leading to Equation 2 and from it to the solution for $P(\mu_0 \mid \mu,\ t)$ must be omitted. A more complete mathematical treatment will be given elsewhere (3). Our present concern is only with the stationary state of fluctuation that is approached after a sufficiently long time:

$$P(\mu) = \lim_{t\to\infty} P(\mu_0 \mid \mu,\ t) = (2\pi\sigma^2)^{-1/2}\, e^{-\mu^2/2\sigma^2} \tag{3}$$

with

$$\sigma^2 = D/g \tag{4}$$

Equation 3 gives the distribution of values around a mean, m, that would be observed in a series of measurements on a single individual, or in a set of measurements on the members of a homogeneous population (as defined above), if the variable being measured had Equation 1 as its equation of motion. The stochastic properties of more complicated dynamical systems can also be analyzed (2).

If there is on one side of the mean, m, a limit value, L, such that every individual whose state fluctuates to or beyond it is removed from the population, then the frequency distribution must go to zero for all $x \geq L$. This determines the modified stationary frequency distribution, $Q(\mu)$,

$$Q(\mu) = (2\pi\sigma^2)^{-1/2}\{e^{-\mu^2/2\sigma^2} - e^{-(2\lambda-\mu)^2/2\sigma^2}\} \tag{5}$$

where $\lambda = L - m$.

From this distribution the rate at which members are removed from the population can be shown to be

$$\rho = -\frac{D}{\int_{-\infty}^{\lambda} Q(\mu)d\mu}\left(\frac{\delta Q}{\delta \mu}\right)_{\mu=\lambda} \tag{6}$$

for $\lambda > 2\sigma$ this can be written to a sufficient approximation as

$$\rho = \frac{g\lambda}{\sigma}\left(\frac{2}{\pi}\right)^{1/2} e^{-\lambda^2/2\sigma^2} \tag{7}$$

where $1/g$ is the mean relaxation time, or mean recovery time of the system, defined by Equation 1, and σ^2 is the variance of the distribution of x, given by Equation 4.

The essential property of Equation 7 is the exponential dependence of rate of

mortality on the magnitude of λ^2 (σ and g are assumed constant). This type of functional relation is given by a large class of stationary Gaussian stochastic processes.

In radiation injury or aging, the state of the organism (and of the population) varies as a function of time. We are concerned here only with the slowly changing processes of aging and chronic radiation effect. There is experimental evidence that for such processes the physiologic changes that occur are shared for the most part by all members of the population, so that they can be represented in a first approximation by a change in the mean state, which thereby becomes a function of time, $m(t)$. Thus λ also becomes a function of time, $\lambda(t)$. The restriction is also imposed that the range of values of λ throughout the process (from irradiation to complete dying-out of the population) is small compared to the magnitude of λ:

$$\langle \Delta\lambda \rangle_{\max} \langle\langle \lambda_0 + \Delta\lambda = \lambda \qquad (8)$$

Under these restrictions, λ^2 can be replaced by the linear terms of an expansion

$$\lambda^2 \simeq \lambda_0^2 + 2\lambda_0\Delta\lambda \qquad (9)$$

After making this substitution and taking logarithms of both sides, we finally have

$$\log \rho\,(t) \equiv G(t) = \frac{\lambda_0}{\sigma^2}\,\Delta\lambda + C \qquad (10)$$

where C is a lumped constant term. Equation 10 is a statement of what can be said at present about the relation of mortality to physiologic state. It states that *the logarithm of the rate of mortality is a linear function of the mean physiologic state of a homogeneous population*. The logarithm of the rate of mortality is henceforth called the Gompertzian and denoted $G(t)$.[5]

APPLICATION TO THE ANALYSIS OF RADIATION MORTALITY[6]

First, let us consider the dependence of natural mortality on age in mammalian populations. Benjamin Gompertz pointed out more than a century ago that the rate of mortality increases exponentially with age (4). This presented a paradox of long standing, for the great majority of observable physiologic variables do not change exponentially by many orders of magnitude during the life span. This paradox can now be resolved, for, according to the relationship exhibited in Equation 10, the gradual linear trend by which most physiologic characters are observed to change with age (5) is sufficient to account for the approximately exponential increase of mortality rate with age. However, a linear increase of $G(t)$ with age is not a necessary consequence of the theory, for there is no reason why age changes in physiologic processes must necessarily be linear.

It is an established fact that, following the acute period of radiation injury in mammals, there is a residue of injury that persists throughout subsequent life. Since this residue is independent of time, it should then produce in the irradiated population a mean physiologic state that differs from (*i.e.*, is worse than) that of the control population by a *constant* amount throughout the remainder of life. If the Gompertzian transformation of mortality rates is indeed a linear measure of physiologic state, then it follows that the plot of Gompertzian values *versus* age for a population given a single radiation dose early in life should be displaced above a similar plot for controls by a *constant* amount at all ages subsequent to the period of acute injury.

The agreement between the theoretical expectation and experimental observation may be seen in Figure 2, which presents a plot of Gompertzian values (presented as mortality rates on a logarithmic scale) from data reported by Furth *et al.* on the survival of male and female LAF_1 mice for 30 months following exposure to single dosages of weapon-quality gamma radiations (6). The agreement of the data with the hypothesis of parallelism of the Gompertz lines is satisfactory by Chi-square test. This

[5] Logarithms to the base 10 are used for all subsequent calculations.

[6] The computations leading to the graphical and numerical results in this section were done in collaboration with Mr. Robert Schweisthal. Detailed description of the numerical analysis will appear separately.

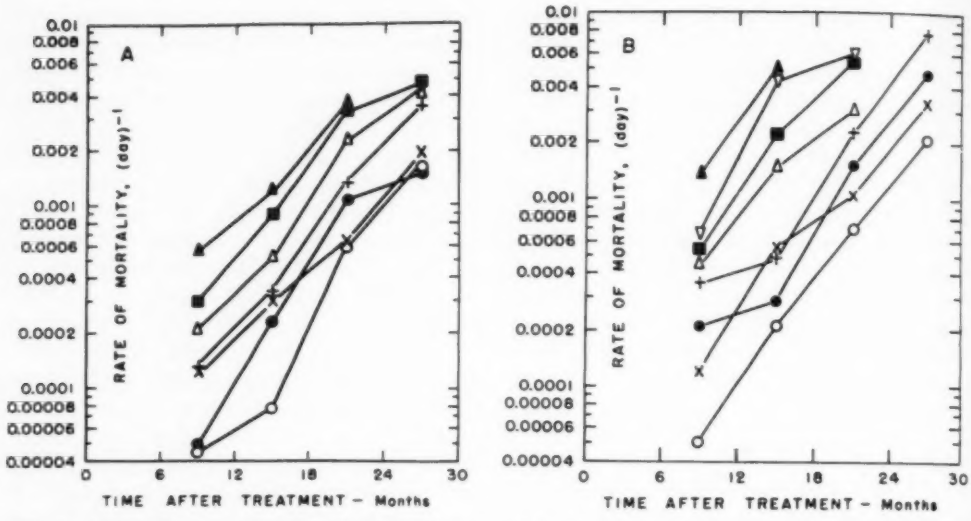

Fig. 2. Age-specific rates of mortality for LAF_1 mice exposed at an average age of sixty-three days to single dosages of gamma radiation; plotted on a logarithmic scale *versus* time after irradiation. Mortality rates, ω_t, calculated as

$$\omega_t = \frac{1}{2h} \log_e \frac{N(t-h)}{N(t+h)}$$

where $2h$ is the time interval and $N(t)$ is the number of animals living at time t.
A. Male mice. B. Female mice.

rule has been found to hold for all lifetime survival data examined.

In view of the demonstration that single doses displace the Gompertz curve upward by a constant amount, the dependence of injury on dose can be completely described by a plot of the displacement *versus* dose. This is done in Figure 3, which is again based on the data of Furth *et al.* (6). The relation of displacement, Y, to dose, D, can be fitted by a quadratic function of the dose over the range of dosages that do not cause heavy acute killing. Evaluation of this relation gives, for male and female mice, respectively,

$$Y_m = 0.016 + 56 \times 10^{-6} D + 1.15 \times 10^{-6} D^2 \quad (11a)$$

$$Y_f = 0.21 + 56 \times 10^{-6} D + 1.15 \times 10^{-6} D^2 \quad (11b)$$

where Y is in units of the common logarithm of the mortality rate.

In the case of the male mouse the amount of permanent injury increases almost as the square of the dose. Data from several other experiments are consistent with this relation. The dependence of delayed mortality on dose is more complicated in the female mouse. In the dose range 200 to 660 r, the curve of displacement *versus* dose for the female is parallel to that for the male, but above it by about 0.2 Gompertz unit. This corresponds to a death rate uniformly higher by a factor of 1.6 than that in irradiated males over this range of dosages. Greater sensitivity of the female mouse with respect to late mortality was also found in several other studies. The existence of a dose-independent component of radiation mortality in female mice given 200 r or more is consistent with the observations of Furth and Boon (7), and of Bali and Furth (8), that a dose of 100 r induces essentially 100 per cent incidence of ovarian tumors in mice. The same dose disrupts the estrus cycle (9) and causes sterility (10) in female mice. The resulting imbalance of endocrine function apparently has reverberations throughout the animal, leading to increased death rates from a variety of causes.

The first-power component of dose-effect

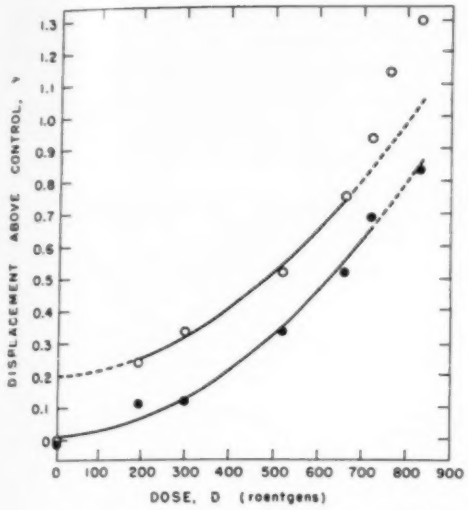

Fig. 3. Relation between displacement of Gompertzian intercept and dose for LAF_1 male and female mice. The continuous curves are described by Equations 11*a* and 11*b*. Solid lines indicate dosage range used in fitting curves. Discrepancies at higher dosages may be due to heavy acute mortality at these dosages. Solid circles, male mice; open circles, females.

cannot be estimated accurately from data on mortality following large single dosages, due to the swamping effect of the second-power term. The first-power term can, however, be estimated with accuracy from data obtained with fractionated or duration-of-life exposures. Figure 4 shows a Gompertz analysis of the data from a fractionation experiment carried out with CF_1 female mice and 250 kvp x-rays (11). The exposure patterns were: single dose of 400 r; 400 or 800 r given as ten fractions in twelve days; and 400, 800, or 1,200 r given as forty fractions in fifty-two days. The analysis is based on mortality rates for all causes of death except lymphoma, which has an unusual time-course of incidence. All of the points of Figure 4 are fitted by the equation

$$Y = 0.256 + 320 \times 10^{-6}D + 1.14 \times 10^{-6}DR\theta\,(1 - e^{-t/\theta}) \quad (12)$$

Here, θ is a time constant for the accumulation of second-power injury, with a numerical value of five days, R is the dose per fraction, and t is the elapsed time of exposure. The second-power term is identical with that given for single dosages above. The first-power term is well estimated in this experiment, and it agrees with an independent estimate based on duration-of-life exposure of CF_1 mice (see below). The constant term for CF_1 females is not significantly different from the value given in Equation 11*b* for LAF_1 females. The first-power term shows no dependence on fractionation, whereas the second-power term has a time-constant of five days.

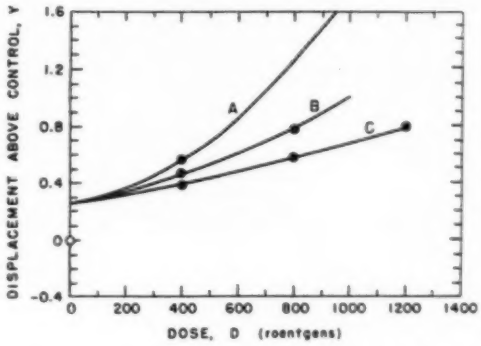

Fig. 4. Relation between displacement and dose for CF_1 female mice given single dosages or fractionated exposures. The three curves are described by Equation 12.

If single dosages cause a step-wise shift of the Gompertz curve, then daily dosages throughout life should cause a linear divergence from controls if the injury due to repeated exposures is a summation of the injury produced by the exposures given separately. This is confirmed by an analysis of the data of Lorenz on LAF_1 mice (12), shown in Figure 5. The Gompertz lines for irradiated groups form a fan of lines. The controls depart from this pattern in that their mortality rates are higher than those of irradiated groups in the early part of the exposure period. This effect is due to an as yet unexplained action of small repeated dosages, which leads to a decreased rate of mortality from infectious disease. We have confirmed the existence of this effect and have it under further study at present (13). If the slopes of the Gompertz lines for irradiated groups are plotted *versus* daily dose, a straight-line relation is found. The slope of this line is an

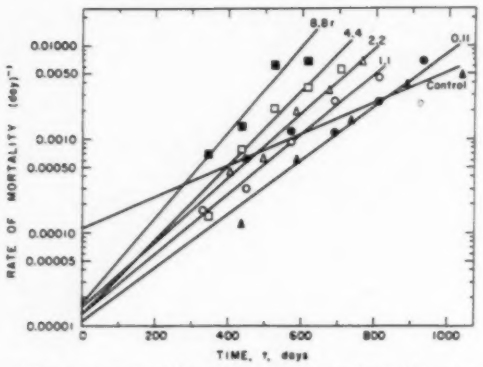

Fig. 5. Age-specific rates of mortality for LAF_1 mice of both sexes that were exposed to radium gamma rays for the duration of life, beginning at about seventy days of age. Mortality rates on a logarithmic scale. Daily radiation dosage indicated for each treatment group. Straight lines fitted by least-squares. A straight line is fitted because it gives a good empirical fit. A straight-line relation of the Gompertzian to age is *not* a necessary consequence of the theory presented here (see p. 253).

estimate of the first-power dose-effect term. The numerical values of the first-power term for the Lorenz LAF_1 mice and for three other daily-dose experiments are summarized in the accompanying table. The first-power term for CF_1 females given single or fractionated dosages was found above (Equation 12) to be $320 \times 10^{-6}\,r^{-1}$. The good agreement between that estimate and the estimate of $339 \times 10^{-6}\,r^{-1}$ from the daily-dose condition supports the inference that the first-power term is non-recovering. The significance of the differences between strains and between radiation qualities in the above table cannot be evaluated as yet.

CONCLUSION

The theory is presented that death is a consequence of the dynamics of physiologic processes. Its occurrence at a particular time in a particular animal is attributed to the prior occurrence of a rare fluctuation of large amplitude in the physiologic state of the animal. By means of a simple mathematical model of a physiologic fluctuation process, it can be shown that the probability of occurrence of such fluctuations is a function of the values of certain vital physiologic parameters. An approximate relation between rate of mortality and mean physiologic state is derived, which states that the logarithm of the rate of mortality is a linear function of the mean physiologic state of a population. Application of this relation to chronic mortality following various patterns of

TABLE I INCREASE OF GOMPERTZIAN (COMMON LOGARITHM OF MORTALITY RATE) PER ROENTGEN, ESTIMATED FOR MICE AND RATS GIVEN DAILY DOSES OF X- OR GAMMA RAYS

Strain	Sex	Quality	First-power Term	Reference
Wistar rat	M, F	X-ray	$303 \times 10^{-6}\,r^{-1}$	(14)
CF_1, mouse	F	X-ray	339 "	(11)
LAF_1, mouse	M, F	Ra gamma	208 "	(12)
C3H mouse	F	Ra gamma	143 "	(15)

radiation exposure yields results that are quantitatively consistent and in accord with present knowledge about permanent radiation injury.

It may be remarked that the dose-dependence of the permanent damage is strikingly reminiscent of the dose-dependence found for induced chromosome aberrations (16, 17). Muller (18) and Lea (19) have given full discussions of the genetic considerations that led them to conclude that permanent radiation injury in mammals must be due primarily to chromosomal aberrations. In view of the indirect evidence presented here, it becomes increasingly important that the role of chromosome damage in late effects be investigated cytologically.

The developments presented here are still far from adequate for the task of prediction that was assigned at the beginning. An attempt has been made to present some concepts that are felt by the author to be fundamental to an understanding of the factors that govern the stability of living organisms. The logical clarification and experimental implementation of these concepts will, however, require much additional work.

REFERENCES

1. The following general references provide an excellent introduction to the subject: Selected Papers on Noise and Stochastic Processes, edited by N. Wax, New York, Dover Publications, 1954 (a reprint of 6

standard papers on the mathematical and physical theory); Symposium on Stochastic Processes, J. Roy. Statist. Soc., Series B, **11**: 150–282, 1949 (contains 2 papers from a biological point of view).

2. WANG, M. C., AND UHLENBECK, G. E.: On the Theory of the Brownian Motion. II. Rev. Modern Physics **17**: 323–342, 1945.

3. SACHER, G. A.: The Stochastic Theory of Mortality. I. The Conceptual Basis and an Illustrative Mathematical Model. In preparation.

4. GOMPERTZ, B.: On the Nature of the Function Expressive of the Law of Human Mortality and on a New Mode of Determining Life Contingencies. Phil. Trans. Roy. Soc. (London), 1825, pp. 513–585.

5. Cowdry's Problems of Ageing, edited by A. I. Lansing, Baltimore, Williams & Wilkins Co., 3rd Ed., 1952.

6. FURTH, J., UPTON, A. C., CHRISTENBERRY, K. W., BENEDICT, W. H., AND MOSHMAN, J.: Some Late Effects in Mice of Ionizing Radiation from Experimental Nuclear Detonation. Radiology **63**: 562–570, October 1954.

7. FURTH, J., AND BOON, M. C.: Enhancement of Leukemogenic Action of Methylcholanthrene by Pre-irradiation with X-Rays. Science **98**: 138–139, Aug. 6, 1943.

8. BALI, T., AND FURTH, J.: Morphological and Biological Characteristics of X-ray Induced Transplantable Ovarian Tumors. Cancer Research **9**: 449–472, August 1949.

9. NUZHDIN, N. I., SHAPIRO, N. I., PETROVA, O. N., AND KITAEVA, O. N.: Effect of Ionizing Radiations on the Fertility of Mice and the Viability of Their Progeny. Conference of the Academy of Sciences of the USSR on the Peaceful Uses of Atomic Energy, 1955 (translation), pp. 21–31. Washington, D. C., Supt. of Documents, U. S. Govt. Printing Office.

10. SANDERSON, M. H., AND STEARNER, S. P.: The Effect of X-Ray on Fertility in the Female Mouse. USAEC Report ANL 5486, 1955, pp. 53–55.

11. SACHER, G. A., SACKIS, J., AND GURIAN, J. M.: Effects of Fractionated X-ray Exposure on Survival and Disease Incidence in Female Mice. In preparation.

12. LORENZ, E., JACOBSON, L. O., HESTON, W. E., SHIMKIN, M., ESCHENBRENNER, A. B., DERINGER, M. K., DONIGER, J., AND SCHWEISTHAL, R.: Effects of Long-continued Total-body Gamma Irradiation on Mice, Guinea Pigs and Rabbits. In Biological Effects of External X and Gamma Radiation, Part I, edited by R. E. Zirkle, pp. 1–242, New York, McGraw-Hill Book Co., 1954.

13. SACHER, G. A., AND GRAHN, D.: Unpublished observations.

14. BOCHE, R. D.: Effects of Chronic Exposure to X-Radiation on Growth and Survival. In Biological Effects of External Radiation, edited by H. A. Blair, pp. 222–252, New York, McGraw-Hill Book Co., 1954.

15. LORENZ, E.: Personal communication.

16. CATCHESIDE, D. G.: Genetic Effect of Radiation. In Advances in Genetics, Vol. II, edited by M. Demerec, pp. 271–358, New York, Academic Press, 1948.

17. KIRBY-SMITH, J. S., AND DANIELS, D. S.: The Relative Effects of X-rays, Gamma Rays and Beta Rays on Chromosomal Breakage in Tradescantia. Genetics **38**: 375–388, 1953.

18. MULLER, H. J.: Some Present Problems in the Genetic Effects of Radiation. J. Cell. & Comp. Physiol. **35**: Supplement 1, 9–70, 1950.

19. LEA, D. E.: Actions of Radiations on Living Cells. New York, The Macmillan Company, 1st Ed., 1947, pp. 341–344.

20. SMITH, W. W., MARSTON, R. Q., RUTH, H. J., AND CORNFIELD, J.: Granulocyte Count, Resistance to Experimental Infection and Spleen Homogenate Treatment in Irradiated Mice. Am. J. Physiol. **178**: 288–292, August 1954.

21. BRUES, A. M., AND RIETZ, L.: Acute Hematologic Radiation Response of the Guinea Pig as a Function of Lethality. USAEC Report ANL 4227, 1948, pp. 183–187.

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SUMARIO

De la Naturaleza Estadística de la Mortalidad, con Referencia Particular a la Producida por la Radiación Crónica

Ofrécese la teoría de que la muerte es consecuencia de la dinámica de los procesos fisiológicos. Se atribuye su ocurrencia en un momento dado en un animal dado a la ocurrencia anterior de una fluctuación rara de mucha amplitud en el estado fisiológico del animal. Por medio de un sencillo modelo matemático de un proceso de fluctuación fisiológica, cabe demostrar que la probable ocurrencia de dichas fluctuaciones constituye una función de los valores de ciertos parámetros fisiológicos vitales. Se deriva una relación aproximada entre el coeficiente de mortalidad y el estado fisiológico medio, que expresa que el logaritmo del coeficiente de mortalidad es una función lineal del estado fisiológico medio de una población. La aplicación de esta relación a la mortalidad crónica consecutiva a varias formas de exposición a la radiación arroja resultados que son cuantitativamente compatibles y concuerdan con los conocimientos actuales acerca de las lesiones permanentes por irradiación.

(For Discussion, see following page.)

DISCUSSION

Henry Quastler, M.D. (Argonne, Ill.): I am much impressed with this paper. It has enormous implications. For one thing, recognition of the possibility of a linear dose-effect relation being associated with a sharp increase in death rate is, I believe, a blessing for all those who try to analyze radiation lethality.

At the beginning of Mr. Sacher's talk he announced what I am sure is a very rational intention, namely, to go from radiation lethality to various physiological changes, and to use those physiological changes to make inferences from animals to man. I think that is fine, but I have not seen this procedure in his analysis. He showed that in irradiation experiments a certain dose is equivalent to passage of a certain number of days as far as the Gompertzian goes; from that he went into a very beautiful general analysis of data. I would like to ask Mr. Sacher: What physiological properties would you look for in animals? Specifically, what properties do you think are involved in the parameters of the equations you had on the slides?

Mr. Sacher: I am sorry to say that we are not yet able to carry out the complete sequence of inferences that is required for the interspecies prediction of radiation lethality. Chronic radiation mortality is not the best starting point for such an attempt, in view of the obscure nature of the late radiation injury, and also of the complications introduced by the aging process, which is an enormous problem in itself. However, the theory can also be applied, in a somewhat more general form, to the acute radiation mortality process, and we are at the present time carrying out experimental and theoretical investigations toward the end of establishing quantitative relations between injury and lethality in the period of acute and subacute injury.

As to the physiological properties one must know, it is of course necessary to know what are the sensitive systems, and what is the average time-response curve, dosage sensitivity, etc., for each system. Some of these characteristics have already been well determined for one or more species. Equally important, however, is a knowledge of the variability of response for each system.

The parameter σ in the above treatment is related to the standard deviation that we estimate to describe the dispersion of a set of measurements on an animal or a population. The empirically estimated dispersion consists, in general, of variation within the animal (fluctuation), variation between animals, and errors of measurement. Accurate estimation of these several components requires carefully devised experiment designs. The parameter g (page 252) is a relaxation rate, or rate at which fluctuations disappear. It is one of several kinds of time constants that specify the performance of homeostatic mechanisms. These are the most difficult parameters of all to identify and estimate, as is evident from the fact that an adequate knowledge of these is tantamount to knowing the dynamical nature of all the essential homeostatic mechanisms. It was with this in mind that I remarked earlier that the implementation of the theory will require much effort.

G. Failla, Sc.D. (New York, N. Y.): In many of the chronic experiments with animals there is a great deal of information about blood counts. Is there any correlation between that physiological reaction and mortality according to your view of the problem?

Mr. Sacher: At this time I can only refer to the work of Willie Smith and her group on acute mortality in mice, showing a considerable predictive value for the neutrophil counts of individual animals within a treated population (20). The animals with the lowest neutrophil counts were found to be most likely to succumb. The lymphocyte level was not prognostic of survival. The correlation of acute LD 50 with neutrophil sensitivity between species is also significant, but it has not received systematic study (21). We are trying to continue investigations of this sort and extend them to other variables and to chronic mortality. As to the important physiologic variables for highly fractionated or protracted exposure patterns, there we must wait for clues from further experimentation.

An Electronic Position Timer for the Fluoroscope[1]

LEE B. LUSTED, M.D., and EARL R. MILLER, M.D.

As many as 30 per cent of the spot-films taken during fluoroscopy may be improperly exposed if the radiologist merely estimates the exposure time.[2] Before phototimers were used, the spot-film exposure time was determined by measuring the thickness of the abdomen. It occurred to one of the authors (E. R. M.) that the fluoroscopic table top and the fluoroscopic screen mounting could be used as a calipers to measure patient thickness. From the measurement thus obtained, optimum spot-film exposure time could be determined. It is the purpose of this paper to describe a method for construction of a spot-film exposure time scale based upon abdominal thickness and to present an electronic timer which uses this scale to control spot-film exposure.

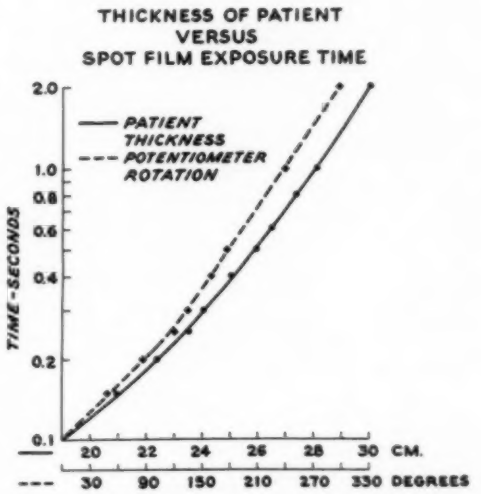


Fig. 1. The electronic position timer action (potentiometer rotation curve) follows closely the optimum exposure time curve.

THE TIME SCALE

An optimum spot-film exposure time, giving a film density and contrast most pleasing to the radiologist, can be determined from the thickness of the abdomen for each patient. On this basis, it becomes possible to construct a scale of optimum exposure times in relation to abdominal thickness for any particular fluoroscope. The fluoroscope used by the authors had the following characteristics: 90 kv, 150 ma, 2 mm. Al filter, 18-inch target-table top distance. For a patient with an abdomen 19 cm. thick an exposure time of 0.1 second was required for an optimum gastrointestinal series or barium-enema spot-film. An abdomen 30 cm. thick required an exposure time of 2 seconds. Spot-films were made at several other abdominal thicknesses between these two points, and a curve was plotted of patient thickness *vs.* exposure time (Fig. 1). This curve is actually the sum of two curves: (*a*) an exponential curve and (*b*) an inverse-square-law curve. The quantity of x-ray energy which reaches the spot-film is a function of patient thickness and the distance of the film from the x-ray source. The exponential curve is concerned with patient thickness. The inverse-square-law curve is related to the target-film distance.

From the graph reproduced in Figure 1, a time scale was constructed. This scale was attached to the fluoroscopic tower and a scale indicator was fastened to the fluoroscopic screen mount. The proper exposure time required for each patient could be read directly from the scale. At the University of California Hospital such a scale was used successfully for a period of months prior to the installation of a phototimer. Before the scale was used, a large fraction of the fluoroscopic spot-films were unsatisfactory as a result of

[1] From the Department of Radiology, University of California School of Medicine, San Francisco Calif. Accepted for publication in August 1955.

[2] Schatzki, R. H.: Personal communication.

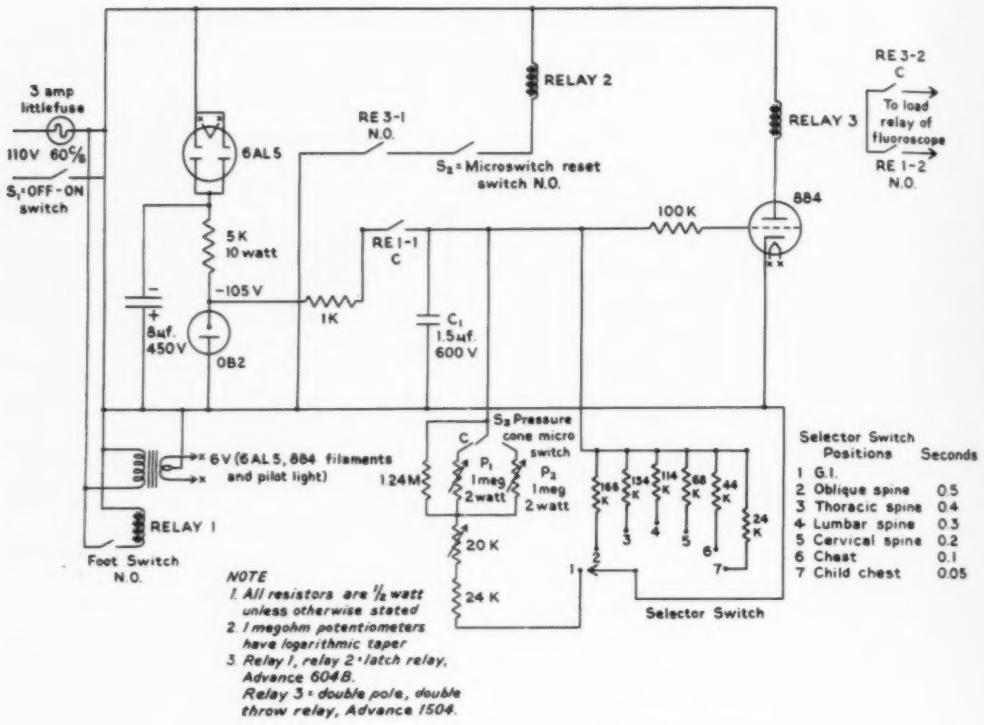


Fig. 2. Circuit diagram of electronic timer for the fluoroscope.

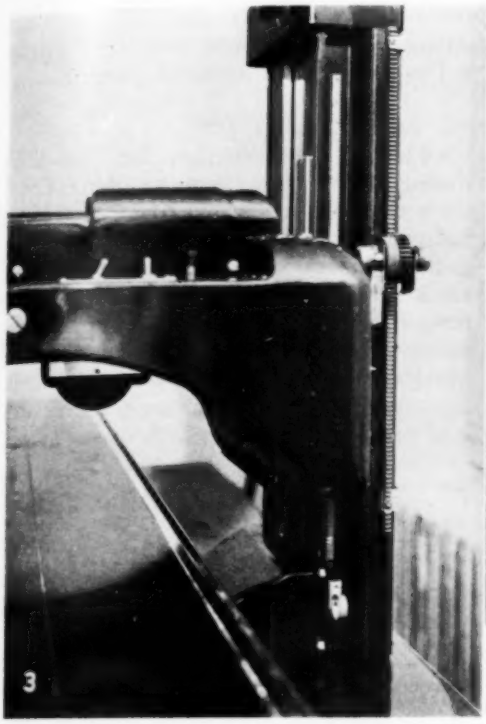
improper exposure. After installation of the time scale, no films had to be discarded for this reason.

THE ELECTRONIC SPOT-FILM TIMER

A simple electronic timer was constructed to adjust automatically the spot-film exposure time in accordance with the time scale just described. The circuit diagram is shown in Figure 2. This timer uses a variable resistor in a resistor-condenser timing circuit. The R-C circuit is attached to the grid of an 884 gas tube. The value of the variable resistance P_1 is determined by the patient thickness as described below.

A potentiometer with logarithmic taper was attached to a pinion gear. The potentiometer and pinion gear were mounted on the movable fluoroscopic screen support (Fig. 3). A rack was attached to the non-movable fluoroscopic screen tower. The potentiometer was fixed in the minimum resistance position at a distance of 19 cm. above the table top. When the fluoroscopic screen was elevated, the pinion gear rolled on the rack and the potentiometer shaft rotated. Thus the value of the resistance was changed with fluoroscopic screen position. The diameter of the gear was determined from the graph of patient thickness versus exposure time. A gear was chosen whose circumference was equal to the distance of travel between 19 and 30 cm. This meant that in one rotation of the gear and potentiometer the spot-film exposure time varied from 0.1 to 2.0 seconds. Figure 1 shows how closely the electronic timer follows the optimum spot-film exposure curve.

The operation of the electronic circuit is as follows: At the time that the spot-film exposure begins, the grid circuit to the 884 gas tube is opened. This allows the grid voltage to increase exponentially according to the R-C value in the grid cir-



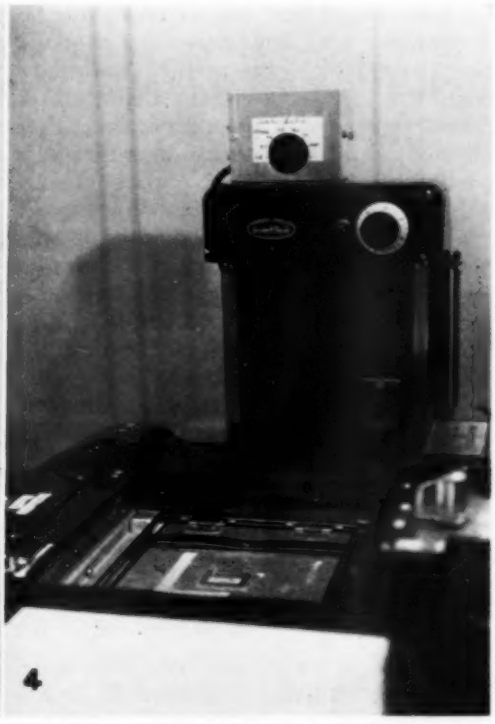


Fig. 3. Rack and pinion gear (at right of photograph) with attached potentiometers mounted on the fluoroscope.
Fig. 4. Control box for position timer, readily accessible on the fluoroscopic screen tower.

cuit. When the grid voltage has reached the critical value of minus 18 volts, the tube fires. As a result, the 884 draws enough current to activate Relay 3 in the plate circuit of the tube. Relay 3 controls the x-ray tube high-voltage relay. Relay 3 contacts are opened when the 884 fires, and the spot-film exposure is terminated.

Some simple additions to the basic timer circuit will increase the usefulness and convenience of the device. A third potentiometer may be added for use with chest fluoroscopy. This third "ganged" potentiometer is easily calibrated for chest thickness, and with it the radiologist will obtain optimum chest spot-films. Fixed value resistors may also be used which will permit the radiologist to make spot-film exposures of predetermined length.

It is convenient to have predetermined exposure values for some types of fluoroscopic examinations. For example, with such values good myelogram spot-films may be obtained. We found that an exposure time of 0.3 second gave an optimum postero-anterior spot-film for a lumbar myelogram. A selector switch (Figs. 2 and 4) will permit the radiologist to choose for various types of examinations the appropriate variable time scale or predetermined spot-film exposure time value.

Three features of the unit should be noted. (1) Relay 2 is a latch-type relay, which does not allow double exposures to be made. (2) The selector switch and six resistors permit the choice of fixed spot-film exposure times as shown in Figure 2. The selector switch box was mounted in a convenient position on the fluoroscopic screen support (Fig. 4). (3) A potentiometer, P_2, was added to be used with the spot-film pressure cone. The potentiometer was adjusted to compensate for the thickness of the pressure cone.

Why is the position timer important?

We believe that there is a need for a simple, inexpensive spot-film timer. The position timer fulfills this need. Phototimer operation has been greatly improved in recent years, but a phototimer is a complicated, expensive device in which the possibility of tube failure is always present.

More consistent background density of spot-films is a second advantage of the position timer. A phototimer scans a specific area of fluorescent screen and determines the exposure time from the average density of this area. Obviously, the spot-film background will be much darker if there is a large amount of barium within the phototimer scanning area than with a smaller amount.

The spot-film background density is always the same with the position timer because the exposure time depends upon patient thickness and not upon light gathering from a fluorescent screen.

SUMMARY

Optimum exposure time for spot-films during fluoroscopy can be determined from the thickness of the abdomen of the individual patient. On the basis of such determinations for various abdominal thicknesses, a spot-film exposure time scale has been constructed. An electronic timer which fixes the exposure time automatically in accordance with this scale has also been devised. Its construction and operation are described.

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SUMARIO

Cronógrafo de la Posición Electrónica para el Fluoroscopio

Durante la roentgenoscopia pueden determinarse los tiempos óptimos de exposición para las radiografías instantáneas a base del espesor del abdomen del enfermo dado. Habiendo ejecutado tales determinaciones para varios espesores abdominales, los AA. construyeron una escala de tiempos de exposición que conectaron con la torre fluoroscópica. Con un indicador asegurado al montaje de la pantalla, puede así leerse directamente de dicha escala el tiempo apropiado de exposición.

También se ha diseñado un sencillo computador electrónico para ajustar automáticamente el tiempo de exposición de acuerdo con la escala. Descríbense la construcción y el funcionamiento de este computador del tiempo. Menos complicado y menos susceptible de fracasos que un fotocronógrafo, posee además la ventaja de una densidad más constante del fondo, dado que el tiempo de exposición se basa en el grueso del enfermo más bien que en la luz acumulada de una patalla fluorescente.

Experimental Evaluation of the Physical Characteristics of a 45-MEV Medical Linear Electron Accelerator[1]

C. L. HSIEH, Ph.D., and ERICH M. UHLMANN, M.D., F.A.C.R.

THE SPECIFIC components designed for the therapeutic application of the 45-MEV linear electron accelerator installed at Michael Reese Hospital and the general principles of operation of this apparatus have previously been reported (1). An electron beam was first released from the accelerator tube on March 6, 1954, but measurements of the physical characteristics of the entire system could be carried out only after the magnet system had been designed, manufactured, and installed.

Theoretically, a linear electron accelerator could be designed in such a manner as to produce a practically monoenergetic electron beam of definite size with energy controlled by the amount of input power or frequency. In the present stage of development, however, an external magnet system is required for the control of the energy and other physical properties of the output electron beam. The performance of the entire system depends as much on the magnets as on the accelerator.

In this paper, some basic characteristics of the accelerator itself will be discussed; the principles of design and the measured performance of the magnet system will be explained; finally, experimental results obtained with the composite system will be presented. Only the physical characteristics pertaining to therapeutic applications will be emphasized.

OPERATIONAL CHARACTERISTICS OF THE ACCELERATOR

Briefly, a traveling-wave linear electron accelerator consists of a disk-loaded copper tube in which an electromagnetic wave with a strong axial electric field and a velocity close to that of light is excited. Mounted at the input end of the tube is an electron gun which injects a beam of electrons into the tube along the axis. These electrons are accelerated by the electric field and pick-up energy until they eventually travel in phase with the wave at a velocity approaching that of light; when they reach the output end of the tube, they have acquired their maximum energy, which is approximately proportional to the square root of the input microwave power used to excite the traveling electromagnetic fields.

The injected electrons are uniformly spaced during the injection pulses, but the time phase of the electromagnetic wave varies continuously. The ultimate fate of each electron will therefore depend upon the initial relative phase angle. It can be shown that, for axial electrons with fixed velocity and electromagnetic fields of constant strength, the greatest number of accelerated electrons will assume a certain asymptotic phase angle which determines the peak energy of a long accelerator; other accelerated electrons will assume an asymptotic phase angle between that value and $-180°$ and therefore assume different energies (2).

The energy spectra of our accelerator were determined, and the half-intensity width was found to be broader for lower energies. The spectra were obtained by varying the magnetic field of the analyzing magnet for different energies and registering the output current with an ion chamber while the energy-defining slit was adjusted for 1 per cent energy spread. To minimize the recombination of ions in the chamber, a relatively low beam current was used, and the chamber readings were corrected for the variation of specific ionization with

[1] From the Tumor Clinic of Michael Reese Hospital, Chicago, Ill. Accepted for publication in August 1955.

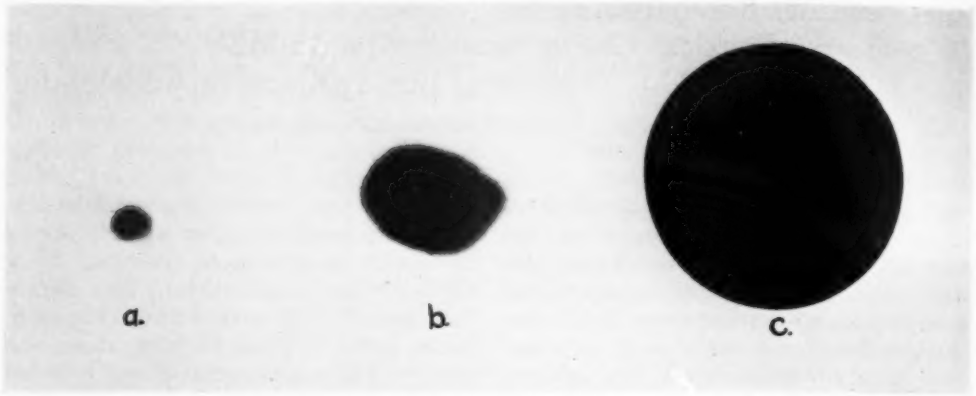

Fig. 1. Photographs of beam size from the accelerator at 30 MEV, obtained close to aluminum window. *a*. Short exposure. *b*. Long exposure. *c*. Size of aperture of loading disks of the accelerator tube obtained with a purposely detuned beam to show proportion.

energy. The corrected ionization reading was then plotted against the magnetic field strength of the analyzing magnet, which in turn was calibrated with photonuclear reaction thresholds and expressed in MEV.

The exact beam shape at the output end of the accelerator is of interest in considering the magnet design. Unfortunately, it is not possible to predict the beam shape on the basis of theoretical calculations, since the initial conditions, *i.e.*, the size, angular spread, and density distribution of the injected electron beam from the gun and the effective field patterns of the electromagnetic waves at the input end of the accelerator, cannot be foreseen accurately. Furthermore, the final beam shape is also influenced by other factors, as the input power, the operating frequency, and the pressure distribution in the accelerator system.

Figure 1 shows film exposures obtained just outside the accelerator aluminum output window when the accelerator was tuned to 30 MEV under normal operating conditions: *a* and *b* are the result of short and long exposures, respectively, but in both instances the distribution of current density over the beam cross section is the same with a half-intensity beam diameter of about 4 mm., as shown in Figure 2. The deviation from a true circular symmetry is probably caused by a misalignment in the horizontal direction. The size of the aperture of the loading disks (about 2.1 cm.) is included in Figure 1 (*c*) for purposes of comparison.

The output current of the accelerator increases with operating energy when the gun injection current is fixed. Curves were obtained by adjusting the input power and frequency for peak output beam current with different magnetic field settings, corresponding to different energies. The target current, *i.e.*, the fraction of the output current from the accelerator which has been analyzed and defocused by the magnet system and which emerges from the transmission ionization chamber, is approximately proportional to the output current of the accelerator, since the energy spectrum is not very sensitive to the operating energy. It can be shown that there exists a linear relation between beam energy and beam current if the tendency toward saturation for high energies, caused by limited electron supply from the gun and beam loading effect, is disregarded. This may be explained by the fact that the beam power (beam current $\times$ beam energy) is equal to the available microwave power for acceleration, which in turn is an approximately constant fraction of the total input power. Also, the square of the beam energy is proportional to the input power

if the beam-loading effect is neglected. Therefore, the obtainable maximum beam current is directly proportional to the beam energy. However, because the fraction of injected electrons which are possibly bound to the wave is also a function of the input power or the operating energy, the above reasoning holds only when the input power is sufficiently high that the fraction of bound electrons is practically constant.

It can be demonstrated that the beam current for a given energy declines sharply when the operating frequency deviates from its optimum value; this is due to the associated change of phase velocity of the accelerating field. A detuning of 0.1 mc out of 2,860 mc reduces the target current to one-half of its maximum value. Since commercial magnetrons ordinarily have a frequency stability in the order of one part in 10^4, it is obvious that a more stable microwave generator is needed if frequent retuning of the magnetron during operation is to be avoided.

Experiments indicate that the beam current is proportional to the gun emission current as long as the latter is sufficiently small that appreciable beam loading is absent.

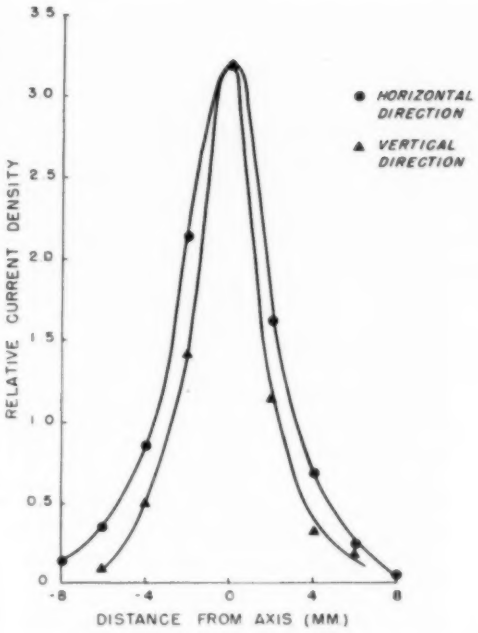

Fig. 2. Current-density distributions over the cross section of the electron beams shown in Figs. 1, *a* and *b*.

MAGNET SYSTEM

Only a brief summary of essential factors, design details, and experimental measurements of the magnet system will be given.

As illustrated in Figure 3, the accelerated electrons, after entering the analyzing magnet, will spread out in a plane parallel to the pole faces of the magnet, depending on the momentum of the individual electrons. Electrons of the same momentum which enter the analyzing magnet with a small displacement off the central trajectory will cross over each other at a point along the central beam; when in the gap-field direction, however, they assume a small divergent angle, caused mainly by the multiple scattering of the accelerator output and the magnet system input windows. An energy-defining slit, whose function it is to confine the energy spread of the electrons which enter the defocusing magnet, is located at this crossing point. It can easily be shown that the fractional energy spread ($\Delta E/E$) of the electrons after passing through the slit is equal to the slit width divided by the effective radius of curvature of the central path of the analyzing magnet.

In front of the energy-defining slit, a block of graphite containing a rectangular tunnel is installed to absorb those portions of the beam which are not utilized and also to limit a definite angular spread in the gap-field direction. The electrons entering the defocusing magnet can be considered as virtually coming from a plane source at the intersection of the projections of incoming and outgoing beams in the analyzing magnet.

The defocusing magnet serves to control the size of the emergent beam at the target plane. Given a fixed entrance and exit angle, the beam dimension in the direction of the accelerator axis is a function of various factors: input collimator size, the energy spread as determined by the

slit opening, and the angular spread in a plane parallel to the pole faces, as a result of the gap-field focusing. In the direction perpendicular to the accelerator axis, the beam dimension depends on the collimator size and the angular spread in the gap-field direction according to the fringe-field effect (3). On the other hand, if all the above mentioned parameters are held constant, then the beam dimensions in both directions will vary only with the entrance and exit angle. In our design, the beam size is controlled by rotating both pole tips of the defocusing magnet. Since the angular spread caused by multiple scattering is energy-dependent, the beam size also changes slightly with the operating energy for fixed magnet settings. The entire magnet system can be rotated electromechanically by 90° about the accelerator axis, so that the direction of the emergent beam can be changed up to 45° from the vertical.

If the calculated and measured beam dimensions at the target plane and their dependence on the exit angle are considered, it appears evident that their variations by gap-field and fringe-field focusing are interdependent. Furthermore, though the beam is uniform and sharply defined along one axis from fringe-field focusing, sharply demarcated beam boundaries are not provided along the other axis by the gap-field focusing because of the energy dependence and the non-uniform distribution of the number of electrons at different energies in the range determined by the slit opening. To improve the field uniformity at the target plane along that

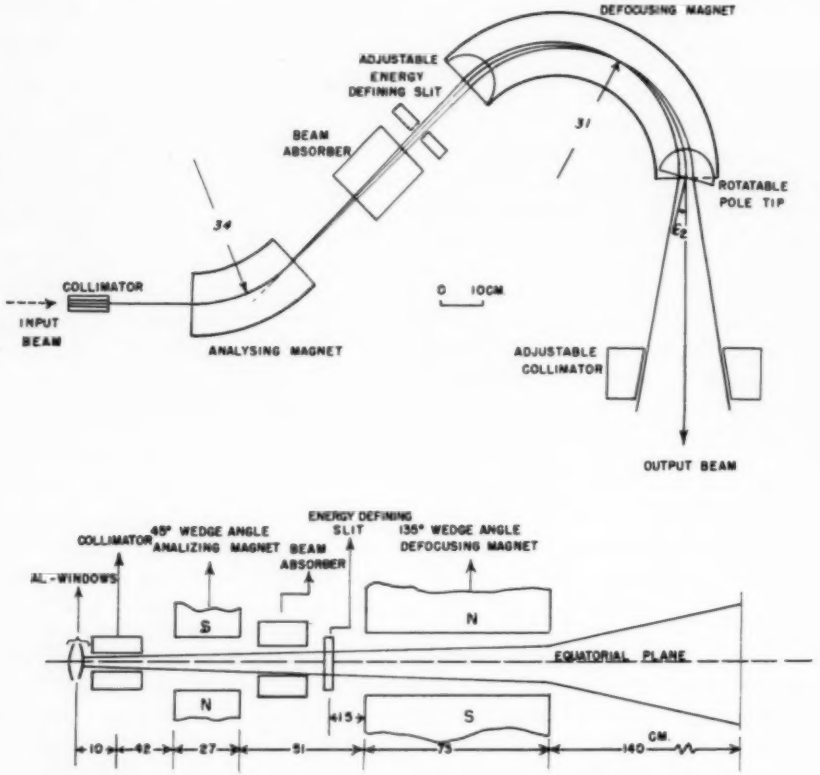

Fig. 3. Schematic diagram of the magnet system. Above: Electron trajectories in the (horizontal) median plane showing gap-field defocusing. Below: Electron trajectories in the stretched-out vertical plane, showing fringe-field defocusing.

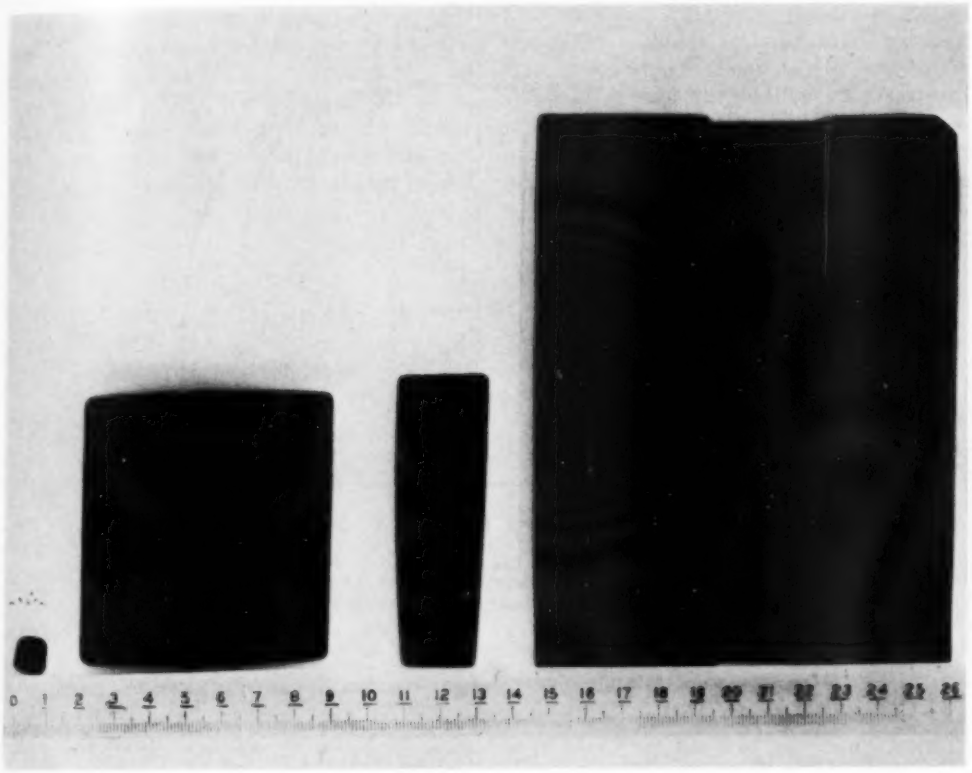

Fig. 4. Some typical field sizes obtained from the magnet system.

axis, a set of adjustable collimators made of graphite is used to cut off the edges of the field.

It is evident from this description that, since the defocusing of the beam is caused by the gap field along one direction and the fringe field along the other, the divergent angles are not necessarily the same in these different directions; the divergent angles also vary with the entrance and exit angles. However, the maximum divergent angle within the designed range of variation of beam size is approximately 3° and, therefore, the emergence of an essentially parallel beam may be anticipated.

Figure 4 shows some typical field sizes obtained with our magnet system. The two slightly tapered edges of the small rectangular field are caused by the finite conductance of the magnetic flux of the pole tips; when the exit angle is large, the fringe field along the edge of the pole tip is no longer uniform and causes variations in the spreading of the beam. No attempt has been made to correct this situation, since it is considered to be desirable for certain applications.

A typical distribution of current density throughout the field, as obtained by the film method, is shown in Figure 5. Kodak industrial "A" film was used, and the exposure was made at a distance of 1 inch from the bottom of the transmission ionization chamber in a plane perpendicular to the emerging beam.

IONIZATION CHARACTERISTICS OF THE ELECTRON BEAM

The distribution of ionization produced by high-energy electron beams has been studied by Skaggs (4) and by Laughlin and others (5) on external beams liberated from

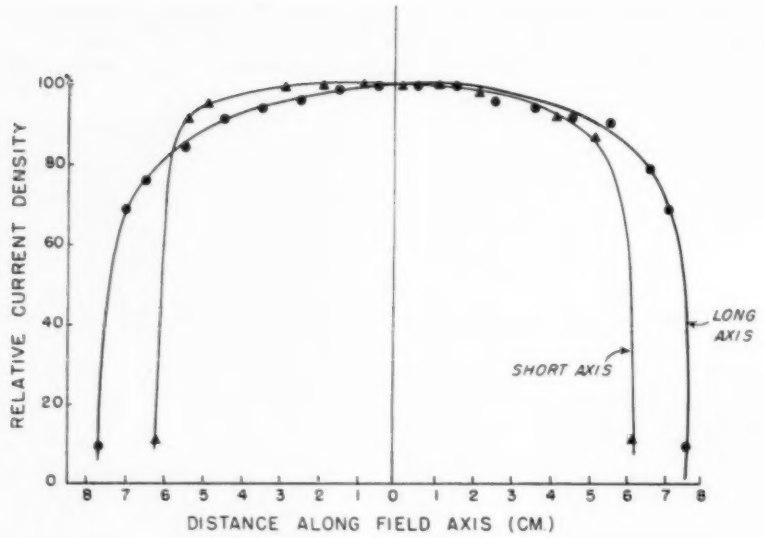

Fig. 5. Field uniformity of a 12 × 15-cm. electron beam of 30 MEV at the target plane (about 6 cm. below the mylar output window of the magnet vacuum chamber and 3 cm. below the transmission ionization chamber electrode).

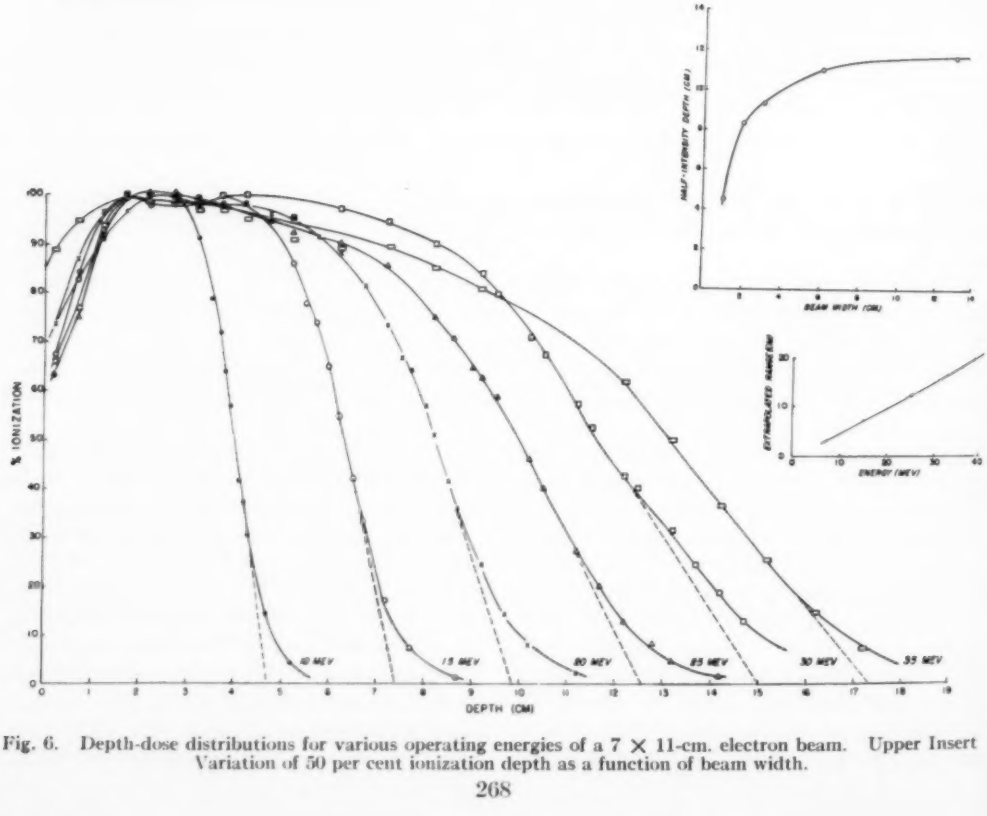

Fig. 6. Depth-dose distributions for various operating energies of a 7 × 11-cm. electron beam. Upper Insert Variation of 50 per cent ionization depth as a function of beam width.

a betatron of 22 MEV maximum energy and by Pollock and his associates (6) with beams from an 80 MEV synchrotron. In the following, depth dose distributions of electron beams produced by the linear accelerator and controlled by the magnet system are presented. Films sandwiched in a Masonite phantom (density = 1.08 gm./c.c.) were used for ionization measurements. The calibration of film density against exposure was carried out at different energies and was found to be independent of energy in the range in which we were interested.

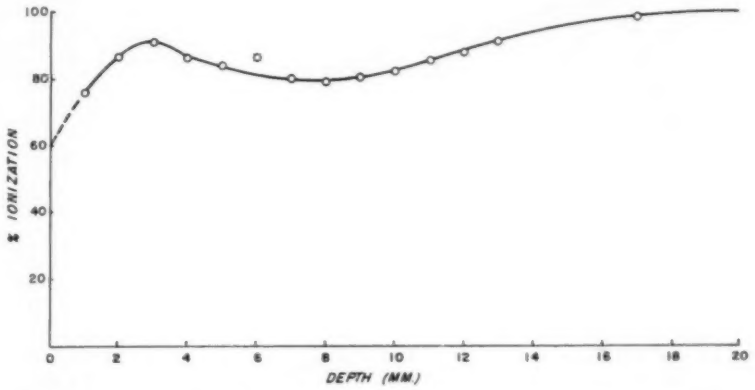

Fig. 7. Variation of depth-dose distribution near the phantom surface of a 30-MEV, 1.8 × 8.2-cm. beam when the magnet system was so adjusted that a large fraction of defocused electrons were intercepted by the graphite collimator.

Figure 6 shows the depth dose distributions for a 7 × 11-cm. field of 2 per cent energy spread obtained with films exposed in the plane perpendicular to the plane of the pole faces of the magnet, the 7-cm. beam width in this plane being controlled by fringe-field focusing. When the difference in densities of the phantom materials are taken into consideration, the extrapolated ranges of electrons of different energies as shown in the insert are essentially in agreement with the observations of the authors mentioned above. Our results, however, indicate a much lower surface dose than those previously reported. This discrepancy can be explained by the fact that either some high-energy x-rays are combined with our beams or that Pollock's and Laughlin's beams contained relatively low-energy electrons (perhaps Compton or pair electrons) or low-energy x-rays (perhaps filtered or scattered primary rays). Such an assumption seems justified by the experiments illustrated in Figure 7. This depth dose distribution is the result of measurements obtained after purposely adjusting the magnet system settings so as to intercept a large fraction of the output beam in the graphite collimator located just above the transmission chamber. The appearance of the first maximum at about 3 mm. from the surface and the subsequent minimum of the ionization distribution clearly indicate the presence of radiations of relatively lower energy. Pollock's curves have a similar tendency except for the absence of the first maximum. It appears probable that his curves might exhibit another maximum near the surface if the aperture of the densitometer were cut down and a careful study made of the variation near the surface.

From a superposition of ionization distributions of x-rays and electrons, it is apparent that an electron beam contaminated with a small amount of relatively low-energy x-rays or electrons tends to give an apparently higher surface dose; if high-energy x-rays are included, a lower

surface dose and a greater extrapolated range will result. The latter situation apparently gives a more favorable dose distribution for deep-seated lesions than utilization of high-energy electron beams or x-ray beams alone. We believe that this mixed-beam therapy is entirely feasible, and a more thorough study of this phenomenon is contemplated.

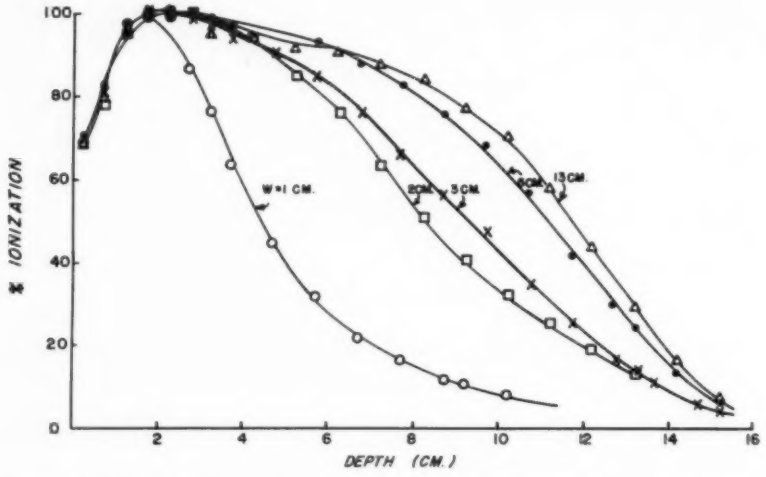

Fig. 8. Variation of depth-dose distribution with beam width (beam breadth = 11.2 cm. energy = 30 MEV).

Determination of the ionization distribution in a medium traversed by an electron beam of given energy is a complex problem, involving the effects of scattering, straggling, radiation loss, variations of specific ionization with energy, etc.; these phenomena defy simple theoretical calculations. Considering the multiple scattering alone, however, one would expect the ionization along the beam axis at any depth within the range determined by the energy of the electrons to increase with the beam size, as the result of the addition of scattered off-axis electrons. This contribution ceases when the beam becomes so large that the half-beam width is greater than the projected range of these scattered electrons. Such a variation of depth dose with beam width for a 30-MEV electron beam of 11.2 cm. constant breadth was observed and is shown in Figure 8 as a typical example. It is interesting to note that, though the extrapolated ranges of these beams, which are of different sizes but of the same energy, tend to meet at the same distance, it becomes increasingly difficult to determine the extrapolated range for narrow beams, due to the constantly varying slope. In Figure 6 (insert) the 50 per cent ionization depth is plotted against the beam width. It is evident that for 30 MEV electrons, when the beam is wider than 6 cm., the axial ionization becomes independent of beam width and an infinite size beam condition is approached. For electron range determinations, a large beam has to be used in order to get accurate results.

Two typical isodose curves, one for a narrow beam and another for a broad one, with the same breadth, are presented in Figure 9, A and B. Here the dependence of ionization distribution on beam width is clearly demonstrated.

STRAY RADIATION SURVEY

The stray radiations of the present accelerator consist of x-radiation due to the unused accelerated electrons, of neutrons produced by photo disintegrations, and of free electrons through Compton

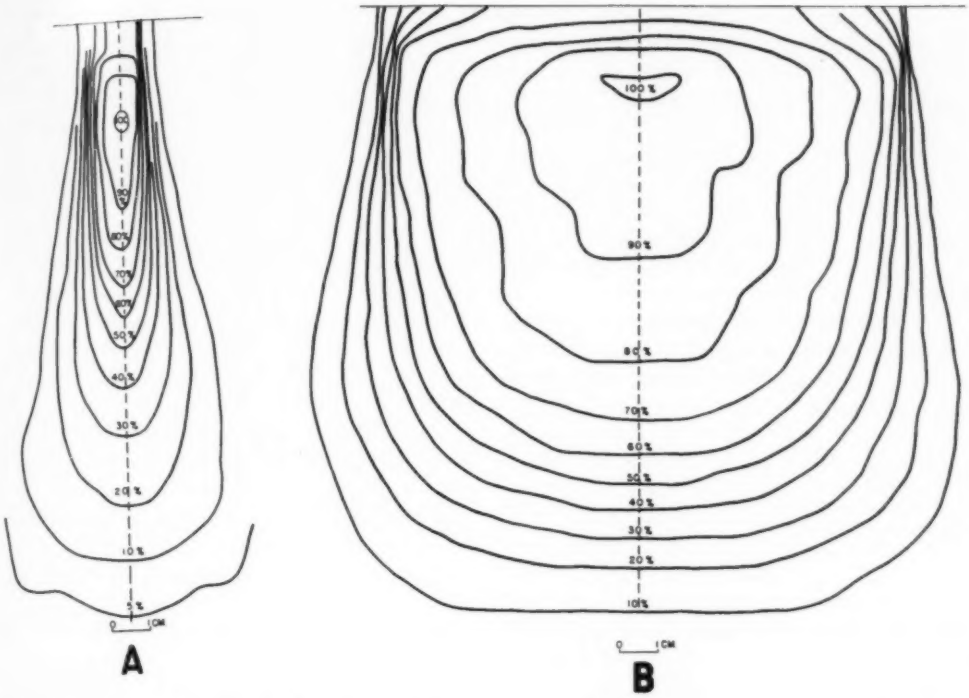

Fig. 9. A. Isodose curve of a 30-MEV, 1.3 × 11-cm. beam in the 1.3-cm. plane. B. Isodose curve of a 30 MEV, 10 × 11-cm. beam in the 10-cm. plane.

effect, pair, and triplet production. The various radioisotopes formed during the operation produce a residual radiation background near the target end of the accelerator with a composite half-life time of thirty-six minutes, though the intensity is insignificant.

By using a deflecting magnetic field on top of the entrance window of an otherwise well shielded ionization chamber, the radiation level of stray electrons in the treatment room was found to be approximately equal to that of the x-radiation. The x-radiation was measured with a Victoreen 25-r chamber embedded in a Lucite block of 2.5 cm. wall thickness as determined experimentally for maximum ionization. The Rh foil activation method was used for measurements of both slow and fast neutrons. For fast neutrons, the foils were exposed inside a paraffin block with a wall thickness of 3 mm. covered with a cadmium shield for thermalization of the fast neutrons and the elimination of external slow neutrons, and the assembly was calibrated with a radium-beryllium source. For slow neutrons, the foils were exposed with and without the shield, and the flux was calculated from the difference of activity between the bare and shielded foil after applying conventional corrections. A G.M. counter calibrated with a UX_2 reference source was used to measure the induced activities.

The results of the radiation survey were tabulated, and all measurements were made after lead pellets of an average thickness of 2 inches were placed for shielding purposes around the accelerator tube and the collimators, and also directly under the magnets. An account of this study has been published (7).

SUMMARY

(1) Essential characteristics of high-energy external electron beams produced

by a traveling-wave linear accelerator were studied experimentally.

(2) The principles of design and the performance of the magnet system used for the control of the energy, direction, and dimensions of the electron beam are outlined.

(3) Depth-dose curves from electron beams of various energies were obtained, and the effect of beam size on the distribution of ionization was studied.

(4) Stray radiations associated with the operation of the accelerator were measured for evaluation of safety during therapeutic applications.

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REFERENCES

1. UHLMANN, E. M., HSIEH, C. L., AND LOOTENS, C. L.: The Linear Electron Accelerator as a Source of Fast Electrons for Cancer Therapy. Radiology **66**: 859–870, June 1956.

2. SLATER, J. S.: The Design of Linear Accelerator. Rev. Mod. Phys. **20**: 473–518, 1948.

3. CROSS, W. G.: Two Directional Focusing of Charged Particles with a Sector-Shaped Uniform Magnetic Field. Rev. Scient. Instruments **22**: 717–722, October 1951.

4. SKAGGS, L. S.: Depth Dose of Electrons from the Betatron. Radiology **53**: 868–873, December 1949.

5. LAUGHLIN, J. S., OVADIA, J., BEATTIE, J. W., HENDERSON, W. J., HARVEY, R. A., AND HAAS, L. L.: Some Physical Aspects of Electron Beam Therapy. Radiology **60**: 165–184, February 1953.

6. POLLOCK, H. C., HEBB, M. H., AND NOBLE, P. C.: The Extraction of the Electron Beam from the 80-Mev Synchrotron. General Electric Report No. RL-546, May 1951.

7. HSIEH, C. L.: The Stray Radiation Levels of a 45-MeV Travelling Wave Linear Electron Accelerator. Brit. J. Radiol. **29**: 201–204, April 1956.

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SUMARIO

Valuación Experimental de las Características Físicas de un Acelerador Lineal Médico de Electrones de 45 Mev

Se estudiaron experimentalmente las características esenciales de haces de electrones externos de alta energía producidos por un acelerador lineal de onda errante. Bosquéjanse los principios del diseño y del funcionamiento del sistema de imanes usado para el gobierno de la energía, la dirección y las dimensiones del haz de electrones. Se obtuvieron curvas de dosis profunda para los haces de electrones de varias energías, y se estudió el efecto del tamaño del haz sobre la distribución de la yonización. Para justipreciar la inocuidad durante las aplicaciones terapéuticas, se midieron radiaciones dispersas enlazadas con el funcionamiento del acelerador.

EDITORIAL

On Professional Medical Liability

A comprehensive current survey of the overall incidence and cost of professional medical liability claims and cases does not exist. Over the past five or six years a number of partial studies and articles have been published but the dissimilarity of the data makes more than a rough correlation of these impossible. The Law Department of the American Medical Association is presently undertaking studies that should aid in broadening our understanding of medical, legal, and insurance aspects of professional medical liability, but these are not as yet available.

This is not to say that we are in complete ignorance. We can use the facts that are known and from these draw inferences that are likely to be valid. While they may not be perfect, they can be used as guides to conduct and action. An instance of this process is to be found in a brief study of closed professional liability insurance claim files involving radiation therapy. It is to be emphasized that none of the observations and conclusions are medical in nature; they concern only the legal or insurance aspects of the material available.

Approximately 55 per cent of the physicians involved were Diplomates of the American Board of Radiology. Of the 45 per cent who were not Diplomates, 7 per cent specialized in Radiology. Payments to claimants followed an identical ratio.

About 23 per cent of the claims involved the treatment of cancer and 66 per cent the treatment of non-malignant conditions. In 10 per cent of the claims the malignant nature of the lesion treated was doubtul.

In the group of claims involving non-malignant conditions, the treament of plantar warts was involved in 27 per cent, of other warts in 25 per cent, dermatitis in 19 per cent, tinea capitis in 10 per cent, and other lesions in 18 per cent.

These bare figures prove nothing, but allow us to infer that the insuring of radiologists for radiation therapy liability costs an insurance company approximately as much as similarly insuring physicians who are not Diplomates of the American Board of Radiology. This is probably because the radiologist's experience is offset by his use of higher exposures; he treats more patients with larger doses more often than do other physicians.

The treatment of non-malignant conditions seems to present a greater professional liability hazard than treatment of cancer. This would be particularly true in the case of the radiologist whose use of radiation is preponderantly in the field of cancer therapy.

In this connection, one may at least wonder as to the implications of the recent National Academy of Sciences Report on radiation effects on the present generation and progeny. Where will the physician stand, legally, who has used radiation in therapeutic dosages for a non-malignant condition on a young parent whose subsequent offspring is defective? Is a mutation involved? If so, was it caused by radiation, and was it the medical radiation rendered by Dr. Doe? Did Dr. Doe explain to the patient—and to the patient's spouse—all possible consequences, including possible effects on future generations? Did both patient and spouse consent to the procedure after gaining a full understanding of the potentialities? These are questions that may arise

A detailed review of individual claims in the group studied allows certain further observations and conclusions.

A radiologist delegates the checking of

filters and dosage factors at his peril. Five of the largest claims resulted from what proved to be an unwise delegation to nurses or technicians. Legally speaking, in the absence of very special circumstances, it would seem that good procedure would be for the radiologist and a technician to check all factors and record them on separate sheets, or to have one record them and the other check and initial this record. If treatments are given by a nurse or technician and are not so checked by the radiologist or, what is worse, are given in the radiologist's absence, imperfect results of treatment may well produce a claim very difficult to defend.

Lack of treatment records, or even poor and incomplete records, make it most difficult to refute liability in the face of a radiation reaction.

Lead shielding, particularly in the treatment of children, should be securely placed and the patient should be constantly and carefully observed during treatment. One who is not a physician cannot medically interpret these and similar data, but from the insurance and legal aspects it would seem that radiation therapy requires an attention to detail that can be accomplished only at a cost of time. The radiologist who is rushed and perhaps has an insufficient number of associates is evidently a poorer insurance risk than his colleagues in medicine not so burdened.

Similar incomplete and, in themselves, inconclusive studies and observations bring up other questions and allow us to draw further conclusions.

Is the increased premium required of partnerships equitable? The answer is that it is probably valid, but precisely what represents a fair charge for this coverage is still in doubt. A memorandum of the National Bureau of Casualty Underwriters notes that the limited experience available shows that partnerships have been "targets" for claims and have been greater risks than physicians practicing alone. This memorandum also notes that the additional charge reflects the fact that at law each partner, in addition to being responsible for his own personal acts and those of his employees, is responsible individually for the acts of all other partners and partnership employees. The current American Medical Association studies and statistics being collected by the Bureau from major American insurers should provide a less qualified answer.

What of the practice of insurance companies of soliciting other types of insurance when called upon to consider an application for professional liability protection? Is this an attempt to influence the purchase of unneeded insurance? No. Rather, it reflects the feeling of insurance companies that present rates are not adequate for medical liability insurance. A thirty-two year study in one insurance company, for instance, shows profits recorded in thirteen years and losses in nineteen in so far as this type of insurance is concerned. The net loss for the entire period is only slightly less than two million dollars.

A question frequently asked of insurance men and attorneys has to do with the amount of medical liability insurance a physician should carry. There are underwriters who believe that high limits of coverage invite claims. They can further point to the fact that few settlements or judgments exceed basic $5,000/$15,000 limits. As opposed to this, however, are recent judgments of $215,000 and $210,000. The best opinion of attorneys and insurance counsel seems to be that a physician should carry an amount of professional liability insurance that safely protects his assets. This would seem to be the only safe advice. After all, unless insurance approaches covering potential liability, the individual is in reality his own insurer.

Do residents need professional liability insurance? The answer to this depends somewhat on one's philosophy. The resident normally is not in a financial category that would attract a lawsuit, and it would not be the intention of an attorney to establish liability against a resident in instituting a suit. It has happened, however, that as a case goes on and the others

named—the hospital, practicing physicians, etc.—establish their freedom from negligence, the resident or intern is the only one left from whom the plaintiff can collect. The attorney for the insurance plan of the Medical Society of the State of New York has noted that he has seen these young men pay as much as $7,500 on the installment plan rather than go bankrupt in order to make up a verdict. This is surely undesirable.

Some institutions carry blanket policies that cover the superintendent, paid members of the staff, and residents. In other instances, residents are named in the policy of the physician in charge of the residency program and their personal liability is thus covered. What should be done in this connection and how to accomplish it is an individual problem for the institution and the physicians involved. It is to be borne in mind, however, that the physician's professional liability policy covers only his personal liability for his acts and those of assistants and employees. The personal liability of such assistants and employees for their own acts is not covered unless they are named, and this applies to residents in training. If these individuals are not covered in the physician's policy, that of the hospital, or in personal policies, they are uninsured.

Will the increased premium required for the therapeutic use of radiation be continued? For the present, yes. A recent study in Alameda and Contra Costa Counties in California, a similar study undertaken in Maryland, and experience of the group professional liability insurance program sponsored by the Medical Society of the State of New York indicate, however, that an easing of this load may lie ahead. The New York program, initiated in 1924, has accumulated the most detailed statistical data available, though only for that state. Recently the attorney for this program informed a group of attorneys of state medical associations that experience in recent years with radiation therapy has not been bad and that it is no longer considered a major hazard in New York. It must be noted, however, that New the York plan will insure the use of radiation for treatment purposes only for physicians with special training in radiation therapy.

What of the ever upward rise in premiums? Is it justified? Probably, yes, but experience of the Florida State Medical Association in challenging, before the Insurance Commissioner of that state, a request for an increase in premiums might well be duplicated elsewhere. The normal procedure has apparently been for companies to apply for such increases with no one appearing to question or resist them. The Florida experience indicates that a full explanation and justification should be required, if for nothing other than its educational value to the medical profession. In Florida, the increases requested were denied because the necessity for them was not proved.

What are the most frequent causes of professional liability insurance claims? A recent American Medical Association survey, in which returns were received from forty-two state medical societies and the District of Columbia, lists the following: imperfect results after orthopedic surgery, radiation reactions, foreign bodies left in the patient after surgery, failure to obtain consent prior to surgery, inaccurate prescription of drugs or improper diagnosis, criticism of one physician by another, excessive fees, and poor physician-patient relationship. This information was gathered in a rough form, so that the relative frequency of these causes is not known.

Other similar studies add to the above list the following: inadequate medical records; failure to explain probable results of treatment; failure to use methods of diagnosis and treatment conforming to the standard of the community; making too optimistic a prognosis or guaranteeing the results of treatment; delegation of duties to unqualified assistants; admitting negligence within the hearing of the patient or members of the patient's family; failure to seek necessary specialized consultation—or consultation with the patient's former physician; except in emergency, examina-

tion of a female patient unless a third person is present; abandonment of a patient, including a failure to advise the patient of any intended absence from practice and notification of the patient in writing of failure to keep an appointment when treatment has been advised. There are still others.

Many of the causes set forth are not strictly medical in nature, but rather concern the relationship between physician and patient as persons. A physician can, by using circumspection and wisdom in his relationship with patients, eliminate a number of these. It would seem that this is where "doing something" about the professional medical liability insurance problem might well start.

WILLIAM C. STRONACH, LL.B.
Chicago, Ill.

ANNOUNCEMENTS AND BOOK REVIEWS

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA SECTION ON RADIOLOGY

The following officers have been elected by the Section on Radiology of the Medical Society of the District of Columbia for 1956–1957: President, David H. Rosenfeld, M.D.; Vice-President, Forest V. Schumacher, M.D.; Secretary-Treasurer, Melvin O. Goodman, M.D., 1930 K St., N. W., Washington 6, D. C.

GEORGIA RADIOLOGICAL SOCIETY

The new officers of the Georgia Radiological Society are as follows: Dr. Robert Tankesley, Atlanta, President; Dr. George Brown, Griffin, Vice-President; Dr. Bert H. Malone, 1406 Reynolds St., Brunswick, Secretary-Treasurer.

NEW YORK ROENTGEN SOCIETY

At a recent meeting of the New York Roentgen Society, the following officers were elected: Dr. Sidney Rubenfeld, President; Dr. Maxwell H. Poppel, Vice-President; Dr. John A. Evans, 525 E. 68 St., New York 21, Secretary; Dr. Harold Jacobson, Treasurer.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The new officers of the Pennsylvania Radiological Society are as follows: President, James M. Converse, M.D., Williamsport; President-Elect, Lewis E. Etter, M.D., Warrendale; First Vice-President, Richard R. Hoffman, M.D., Lebanon; Second Vice-President, John W. Hurst, M.D., Altoona; Secretary-Treasurer, Walter P. Bitner, M.D., 234 State St., Harrisburg; Editor, Carl B. Lechner, M.D., Erie.

PHILADELPHIA ROENTGEN RAY SOCIETY

Newly elected officers of the Philadelphia Roentgen Ray Society are: President, Rolfe M. Harvey, M.D.; Vice-President, Marston T. Woodruff, M.D.; Secretary, Roderick L. Tondreau, M.D., University of Pennsylvania Hospitals; Treasurer, Randal A. Boyer, M.D.

PITTSBURGH ROENTGEN SOCIETY

At a meeting of the Pittsburgh Roentgen Society, held on June 13, the following officers were elected for the ensuing year: President, Newton Hornick, M.D.; Vice-President, Dutney J. Hayes, M.D.; Secretary, N. B. Tannehill, M.D., 601 Jenkins Building, Pittsburgh 22; Treasurer, Harrison H. Richardson, M.D., Rochester.

SOCIEDAD PERUANA DE RADIOLOGIA

Officers of the Sociedad Peruana de Radiologia for 1956–57 are as follows: President, Jorge de la Flor V., M.D.; Vice-President, Enrique Gonzalez Vera, M.D.; Secretary General, Luis Pinillos G., M.D., Apartado 2306, Lima; Second Secretary, Vincente Ubillús, M.D.; Treasurer, Jorge Salazar A., M.D.; Library's Secretary, Guillermo Pezet M.Q., M.D.

SOCIEDAD ESPAÑOLA DE RADIOLOGIA Y ELECTROLOGIA MEDICAS

The new officers of the Sociedad Española de Radiologia y Electrologia Medicas are as follows: President, Dr. Vincente Carulla Riera; First Vice-President, Dr. Francisco Arce Alonso; Second Vice-President, Dr. Manuel Alonso Canalejas; Secretary, Dr. Aureo Gutierrez Churruca; Assistant Secretary, Dr. José M. Vilaseca Sabater; Treasurer, Dr. Francisco Orfila Oterman; Auditor, Dr. Octavio Sales Nicasio; Recording Secretaries, Dr. Enrique Rivera Monreal and Dr. Luis Salvador Gallardo; Librarian, Dr. Julian Gutierrez del Olmo; Members of the Board of Directors: Dr. Ramón Sebastiá Abreu, Dr. Fernando de Castro Garcia-Patón, Dr. Pedro Melendo Abad.

RADIATION STUDY SECTION NATIONAL INSTITUTES OF HEALTH

Because of the recognition of the importance of radiology to the medical and related sciences and its growing influence in scientific pursuits, the *Ad Hoc* Committee on Radiation Studies has been replaced by a full-fledged Study Section on a permanent basis within the framework of the Division of Research Grants, National Institutes of Health. The first meeting of the newly established Radiation Study Section was held in Bethesda, Maryland, in September 1955. Present membership of the group is as follows:

Dr. Howard J. Curtis, *Chairman*, Brookhaven National Laboratory; Dr. Howard L. Andrews, National Cancer Institute; Dr. Charles L. Dunham, Atomic Energy Commission; Dr. Jacob Furth, Children's Cancer Research Foundation, Boston; Dr. Harry Harlow, University of Wisconsin; Lt. Col. James B. Hartgering, Walter Reed Army Institute of Research; Dr. Henry S. Kaplan, Stanford University School of Medicine; Lt. Col. Solomon E. Lifton, U. S. Air Force; Dr. Russell H. Morgan, Johns Hopkins Hospital; Dr James J. Nickson, Sloan-Kettering Memorial Cancer Center; Dr. Harvey M. Patt, Argonne National Laboratory; Dr. J. Paul Quigley, University of Tennessee; Dr. Cornelius A. Tobias, University of California; Dr. J. Walter Wilson, Brown University; Dr. Raymond E. Zirkle, University of Chicago.

Study Section members have two major responsibilities: (1) to review applications for research grants and provide technical advice on action to be taken and (2) to survey the research being conducted in radiation in order to stimulate additional work in neglected areas.

In general, the main interest of the Section is in the field of vertebrate and invertebrate radiation biology and clinical radiology. The group has expressed the need for expansion of investigations in primate radiation research and biological investigations in support of radiation therapy, as well as research on health hazards related to ionizing radiation. With respect to clinical radiation, the Section would like to encourage studies on radiation sources, dosimetry, experimental therapy, and modification of radiation sensitivity. In the field of mammalian radiation there is need for investigation in histologic, physiologic, and developmental changes in the induction of tumors and neuropsychologic aspects.

Based upon discussions of Study Section members and upon types of applications already submitted, there are listed below suggestions of the types of projects that fall within the scope of activities of the section and areas needing investigation. Among these are studies on the effects of radiation on chemical compounds of biological significance, particularly those related to possible mechanisms of radiation effects; the effects of radiation on unicellular organisms and lower life, and vertebrates; effects of supralethal radiation doses; neuropsychologic aspects of radiation; the dose rate variable in biologic effects; field studies on human population groups exposed to greater than normal amounts of radiation; experimental therapy with radiation from various sources; quantitative effects, particularly at low dosages; development of methods to enhance the differential effect of radiation in malignant tissue as compared to normal; development of dosimetry of beta and gamma rays.

Requests for Public Health Service research grant support should be submitted by an institution on behalf of an investigator's proposed research, using special application forms which may be obtained by writing to the Division of Research Grants, National Institutes of Health, Bethesda 14, Maryland. Included with the application will be instructions for its preparation and submission.

JAMES PICKER FOUNDATION AWARDS IN RADIOLOGICAL RESEARCH

The James Picker Foundation has announced the following awards for 1956–57:

Grants in Radiological Research: Dr. John A. Benjamin and Dr. James S. Watson, Strong Memorial Hospital, University of Rochester, for cinefluorographic studies of urinary tract function, normal and abnormal, in man and dog; *Dr. F. X. Gassner and Dr. H. J. Hill*, Colorado Agricultural & Mechanical College, for continued investigation of the angiographic and luminal characterization of the testis and accessory sex organs in relation to fertility in the male; *Dr. Gwilym S. Lodwick*, University of Missouri, for continuation of his studies on the roentgen evaluation of the diagnosis and aggressiveness of primary bone and lung neoplasms; *Dr. Robert J. Reeves*, Duke University, for continued studies on the effects of roentgen irradiation upon digestion and absorption of materials in the gastrointestinal tract by means of radioactive tagged compounds and correlative roentgenological studies; *Dr. Francis F. Ruzicka, Jr., and Dr. Louis M. Rousselot*, St. Vincent's Hospital of the City of New York, for a rapid serial venographic study of the portal venous system; *Dr. H. A. Sissons*, Institute of Orthopaedics, University of London, for continued microradiographic studies of bone structure; *Dr. Michel Ter-Pogossian*, Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, for studies on monochromatic x-rays in contrast media diagnostic roentgenology.

Fellowships in Radiological Research: Dr. Leonard Davis, for an investigation of the uses of a double balloon modified Miller-Abbott tube, under the guidance of Dr. Robert M. Lowman at Grace-New Haven Community Hospital; *Dr. Hans Ludin*, for the development and evaluation of pancreas pneumography, under the guidance of Dr. John A. Evans at Cornell Medical College; *Dr. Vincenzo Valentino*, for a study of the anatomical, angiographic, and encephalographic aspects of cranio-encephalic malformations producing clinical and pseudo-tumoral changes, under the guidance of Dr. Donald McRae at the Montreal Neurological Institute, McGill University.

Scholar in Radiological Research: Dr. William J. Tuddenham, University of Pennsylvania School of Medicine, for continuation of his investigation of the physiologic optics of roentgen interpretation.

ARMED FORCES RESERVE MEDICAL OFFICER COMMISSIONING AND RESIDENCY CONSIDERATION PROGRAM

Attention is called to a recent *Bulletin* describing the "Armed Forces Reserve Medical Officer Commissioning and Residency Consideration Program," known also as the Berry Program. This program has been developed to permit physicians who are liable for military service to be commissioned well in advance of the time they are required to serve and to permit successful applicants to be deferred for residency training in specialties required by the Armed Forces. To participate in the program, one must be a 1956 graduate of an approved medical school (United States or Canada), be liable for two years of military service, and be willing to accept a Reserve commission in the Army, Navy, or Air Force.

The *Bulletin* is issued by the Office of the Assistant Secretary of Defense (Health and Medical), Washington 25, D. C.

Letter to the Editor

To the Editor of Radiology

DEAR DR. DOUB:

This morning I examined a patient for whom a "complete G-I" had been requested. I believed that the doctor desired an examination of the colon and of the esophagus, stomach, and duodenum. My technician suspected that the referring physician also wished a study of the small bowel.

Past experience, during medical training in Montreal, Winston-Salem, Durham, N. C., and in Wisconsin, Minnesota, and Oregon, as well as in the Army Medical Corps, has impressed upon me that "G-I study" and similar terms may mean so many different things that it is time for reappraisal. It would be ideal if physicians requesting roentgen studies would themselves write out in detail what they desire, but we know this ideal will not be attained. Requests for studies are made over the telephone and are scribbled on prescription sheets.

I believe it would help if our radiological societies would adopt a standard nomenclature and recommend it to Blue Shield and other doctor-owned medical care plans as well as to Blue Cross, welfare organizations, and private insurance carriers. I would recommend that the term "G-I series" be discarded and would suggest the following abbreviations for a start:

(1) A.C.E. Air-contrast enema for double-contrast colon study.

(2) Cholangiograms. (*a*) I.V. Cholangiogram. Intravenous cholangiogram. (*b*) Operative Cholangiogram. A cholangiographic study, under sterile conditions, in surgery, where the medium is injected by the surgeon during celiotomy. (*c*) Postoperative Cholangiogram. Contrast medium injected in the x-ray department through a drainage tube, following surgery.

(3) Colon. Ordinary barium enema examination.

(4) E.S.D. Fluoroscopic and film study of the esophagus, stomach, and duodenum.

(5) G.B. Oral cholecystography only.

(6) S.B.E. Small bowel enema. A limited quantity of barium or other opaque medium is introduced directly into the small bowel through a tube which must be (or already has been) passed into the duodenum or beyond. Fluoroscopic and film studies.

(7) S.B.S. Small bowel study. This examination requires a barium swallow. The radiologist will employ fluoroscopy and radiography as he deems necessary for adequate study of all portions of the small bowel and recognition of any abnormality manifested during the passage of barium throughout the small bowel into the colon.

The above suggestions are not expected to meet with general approval. I am convinced, however, that it is time to reject the use of careless terminology which produces confusion and sometimes genuine misunderstanding. I find the abbreviation E.S.D. particularly useful, easy of adoption, and free of troublesome associations. Perhaps with this expression of opinion, others will submit more useful suggestions and we can arrive at a standard nomenclature which all radiologists will be happy to adopt and suggest for adoption to other physicians and insurance carriers.

Very truly yours,
DONALD BAUER, M.D.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

BORDERLANDS OF THE NORMAL AND EARLY PATHOLOGIC IN SKELETAL ROENTGENOLOGY. By PROF. DR. ALBAN KÖHLER. Tenth Edition, completely revised with reference to illustrations and to text by Dozent Dr. E. A. ZIMMER, Bern/Fribourg. English translation arranged and edited by JAMES T. CASE, M.D., D.M.R.E. (Cambridge), Professor Emeritus of Radiology, Northwestern University Medical School, Chicago; Director, Memorial Cancer Foundation, Santa Barbara, Calif. A volume of 724 pages, with 1,300 illustrations. Published by Grune & Stratton, Inc., New York and London, 1956. Price $24.50.

ORAL CANCER AND TUMORS OF THE JAWS. By GEORGE S. SHARP, M.D., F.A.C.S., F.A.C.R. (Ther.), Professor of Pathology, School of Dentistry, Assistant Clinical Professor of Surgery, School of Medicine, University of Southern California, Director, Pasadena Tumor Institute; WELDON K. BULLOCK, M.D., M.Sc. (Path.), Associate Clinical Professor of Pathology, School of Medicine, University of Southern California, Surgical Pathologist, Los Angeles County Hospital; and JOHN W. HAZLET, D.D.S., Lecturer, Oral Tumor Pathology, School of Dentistry, University of Southern California. A volume of 562 pages, with numerous illustrations, including roentgenograms Published by McGraw-Hill Book Company, Inc., New York, 1956. Price $15.00.

RADIATION DOSIMETRY. Edited by GERALD J. HINE, Veterans Administration Hospital, Boston, Mass., and GORDON L. BROWNELL, Massachusetts General Hospital, Boston, Mass. A volume of 932 pages, with numerous figures and tables. Published by Academic Press Inc., New York, 1956. Price $22.00.

BLAKISTON'S NEW GOULD MEDICAL DICTIONARY. A modern comprehensive dictionary of the terms used in all branches of medicine and allied sciences, including medical physics and chemistry,

dentistry, pharmacy, nursing, veterinary medicine, zoology and botany, as well as medicolegal terms; with illustrations and tables. Editors: NORMAND L. HOERR, M.D., and ARTHUR OSOL, Ph.D. With the co-operation of an editorial board and 88 contributors. A volume of 1,464 pages, with 252 illustrations on 45 plates, 129 in color. Published by McGraw-Hill Book Company, Inc., New York, Second ed., 1956. Price $11.50.

THE LUNG AS A MIRROR OF SYSTEMIC DISEASE. By ELI H. RUBIN, M.D., Professor of Clinical Medicine, Albert Einstein College of Medicine, Yeshiva University; Director of Pulmonary Diseases, Bronx Municipal Hospital Center; Attending Physician, Division of Pulmonary Diseases, Montefiore Hospital; Consulting Physician in Pulmonary Diseases, Lebanon and Morrisania City Hospitals, New York, N. Y. A volume of 288 pages, with 92 figures and 11 tables. Published by Charles C Thomas, Springfield, Ill., 1956. Price $12.50.

PRINCIPLES OF CHEST X-RAY DIAGNOSIS. By GEORGE SIMON, M.D., F.F.R., Assistant Director, X-ray Department, Brompton Hospital, London; Radiologist and Demonstrator, Radiological Anatomy, St. Bartholomew's Hospital, London; Curator of the Radiological Museum and Teacher of Radiology, The Institute of Diseases of the Chest, University of London. A volume of 184 pages, with 162 figures. Published by Butterworth & Co. Ltd., London, 1956. Price 50s.

LES TUMEURS DE L'AMYGDALE ET DE LA RÉGION VÉLOPALATINE. By A. ENNUYER and J.-P. BATAINI, Medicins de la Fondation Curie. (Statistiques de la Fondation Curie. Exploitation Statistique by DR. FAUTREL). A volume of 536 pages, with 150 figures and 91 tables. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris-6e. Price 5,000 fr.

CONTRIBUTION À L'ÉTUDE DU SYNDROME ENDOCRINIEN PROVOQUÉ PAR L'IRRADIATION TOTALE DE L'ORGANISME. By E. H. BETZ. Chef de Travaux à l'Université de Liege, Associé du Fonds National de la Recherche Scientifique. Preface by Robert Courrier, Secrétaire perpétuel de l'Académie des Sciences, Professeur au College de France. A volume of 326 pages, with 71 figures. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris-6e. Price 2,800 fr.

STRATITERAPIA BIFOCALE. By G. TORI, G. BRUSORI, R. MICELI, and E. ZAFFAGNINI. Foreword by Prof. G. G. PALMIERI, of the Instituti de Radiologia e del Radio dell'Università di Bologna. A volume of 146 pages, with 59 figures and 3 tables. Published by L. Cappelli, Bologna, 1956.

Book Reviews

ANKYLOSING SPONDYLITIS. CLINICAL CONSIDERATIONS, ROENTGENOLOGY, PATHOLOGIC ANATOMY, TREATMENT. By J. FORESTIER, M.D., F.A.C.R. (Hon.), Aix-les-Bains, F. JACQUELINE, M.D., Aix-les-Bains, and J. ROTES-QUEROL, M.D., Barcelona. Translated by A. U. DESJARDINS, M.S., F.A.C.P., F.A.C.R. A volume of 374 pages, with 145 figures. Published by Charles C Thomas, Springfield, Ill., 1956. Price $10.75.

The treatise on ankylosing spondylitis by Forestier, Jacqueline, and Rotes-Querol published in Paris in 1951 (reviewed in RADIOLOGY **58**: 587, 1952) represented the first comprehensive study of this subject, bringing together in one volume the various aspects of the disease. It is well to have an English edition of this outstanding work, particularly from the hands of so competent a translator as Dr. Desjardins. The authors have themselves made some minor changes in presentation and certain additions to the bibliography to cover the contemporary literature. Otherwise the text is as originally published.

In the reviewer's opinion, this is a most satisfactory compilation of the clinical features of a disease which is encountered in all countries, affecting people of all races. After a brief historical outine for orientation purposes, the authors proceed to a detailed description of the early manifestations and mode of progress of the disease as observed in their 400 cases. The various clinical forms are discussed, and there are sections on etiology and pathologic anatomy. The last 150 pages of the work are devoted to the therapeutic aspects, covering the general medical and orthopedic measures as well as radiotherapy, which has assumed an important place in arresting progress of the condition.

This volume is unhesitatingly recommended to all who are interested in the diagnosis and treatment of arthritis of the spine.

ANNUAL REVIEW OF NUCLEAR SCIENCE, VOLUME 5, 1955. Edited by JAMES G. BECKERLEY, Schlumberger Well Surveying Corporation, MARTIN D. KAMEN, Washington University Medical School, and LEONARD I. SCHIFF, Stanford University. A volume of 448 pages, with numerous illustrations and tables. Published by Annual Reviews, in cooperation with the National Research Council of the National Academy of Sciences, 1955. On sale by Annual Reviews, Inc., Stanford, Calif. Price $7.00.

This fifth volume of the series of *Annual Reviews of Nuclear Science*, the first of which was published in 1952, contains thirteen chapters, written by twenty-two scientists. Contributions come from a number of government institutions, such as the Brookhaven, Oak Ridge, and Argonne National Laboratories and the Los Alamos Scientific Laboratory.

Others are from the Universities of California, Indiana, Purdue, New York, Utah, and Leeds in England. The radiologist will be most interested in the chapter on "Nuclear Particle Detection" (W. B. Fretter), which describes the physical principles of cloud and bubble chambers, and the chapters on "Radiation Chemistry" (F. S. Dainton), "Radiochemical Separation Techniques" (H. L. Finston and J. Miskel), "The Fundamentals of Radioautography" (W. P. Norris and L. A. Woodruff), "Cellular Radiobiology" (R. K. Mortimer and C. A. Beam), "Removal of Radioelements from the Mammalian Body" (J. Schubert), and "Vertebrate Radiobiology: Physiology" (A. Edelmann). Other chapters, as for example "Electromagnetic Transitions in Nuclei," are highly specialized or pertain to the industrial application of nuclear energy.

The high standards both of text and illustrations, characteristic of previous volumes of this series, have been maintained. References are again abundant, averaging considerably more than one hundred per chapter. As a reference source on nuclear science these *Annual Reviews* are invaluable.

ATLAS OF EXFOLIATIVE CYTOLOGY: SUPPLEMENT I. By GEORGE N. PAPANICOLAOU, M.D., Ph.D. Sixteen color plates with descriptive material and instructions for insertion in the Atlas as originally issued. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Mass., 1956. Price $4.00.

In a review of Dr. Papanicolaou's *Atlas of Exfoliative Cytology* appearing in an earlier issue of RADIOLOGY (**63:** 111, 1954), the 36 color plates are described as achieving "a standard of excellence seldom attained by medical illustration in this country." To these, the present *Supplement* adds 16 plates of like high quality, together with concise descriptions and discussions. Fourteen of the plates present comparative illustrations of cells as seen in tissue and in smears, bringing out the similarities and dissimilarities to be observed. The remaining 2 plates are purely cytological. Instructions for insertion of the new material at the appropriate places in the original volume are included.

UROLOGIE DE L'ENFANCE. TRAVAIL DE LA CLINIQUE MÉDICALE DES ENFANTS DE LA FACULTÉ DE PARIS (Professor Robert Debré). By GASTON LAURET, Ancien Interne des Hôpitaux de Paris, chargé de la consultation d'urologie á la Clinique Médicale des Enfants Malades, and Collaborators. Preface by Professor Debré. A volume of 442 pages, with 330 figures. Published by Expansion Scientifique Française, 15, Rue Saint-Benoît, Paris 6e, 1956. Price 3,900 fr.

This is the first French work to appear devoted exclusively to the urology of childhood, reflecting a personal experience of some twenty years in this field. Because of the immediate and wide repercussions of abnormalities in the urinary tract of the child upon the whole body economy, the author has seen fit to make this largely a joint enterprize, and has received aid from his pediatric associates in the field of genetics, metabolism, neurology, and pathology.

The book is divided into three parts: The first deals with the general clinical study of the patient; the second with malformations; the third with acquired conditions, such as those resulting from abnormalities of the central nervous system, urinary lithiasis, urinary tuberculosis, and urinary neoplasms. Diseases of the external genitalia are not considered, since these are adequately handled by the general pediatric surgeon.

The bibliography is predominantly French and Anglo-Saxon.

Typographically the book is well arranged and readable, and the illustrations, with abundant line drawings, are adequate.

TUBERCULOSE UTÉRO-ANNEXIELLE. ASPECTS ACTUELS—DIAGNOSTIC—TRAITEMENT. By JULES BRET, Gynécologue-Accoucheur des Hôpitaux de Paris, and ROBERT LEGROS, Gynécologue-Accoucheur adjoint de l'Hôpital de Créteil, with the collaboration, for pathologic anatomy, of BERNARD DUPERRAT, Médecin des Hôpitaux de Paris, Professeur agrégé à la Faculté de Médecine de Paris. A volume of 248 pages, with 60 figures. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris 6e, 1956. Price 1,600 fr.

This monograph represents a rather complete treatise on female genital tuberculosis based on observations in 100 cases. The body of the uterus and tubes are affected much more commonly than the ovaries and cervix. In the tubes several types of lesions are seen: miliary, ulcero-caseous, and fibrocaseous lesions may occur; hydrosalpinx, hematosalpinx and pyosalpinx may ensue, and chronic nodular and sclerotic changes may lead to retraction or stenosis. In the uterus massive caseous lesions are uncommon, while small tuberculous "follicles" are common.

Hysterosalpingography was found to be a valuable adjunct in diagnosis. Although the authors are apparently not strongly opposed to the water-soluble media, they still prefer Lipiodol. They use "fluid Lipiodol," less viscous than the usual preparation. A control film of the pelvis is taken to ascertain whether calcification is present. Anteroposterior, oblique, and lateral views are used routinely; a film is taken after evacuation of the contrast material, and lateral decubitus or upright views are obtained to demonstrate fluid levels in hydrosalpinx. A twenty-four-hour film is indicated to ascertain whether the tubes are patent and to determine the location of any retained contrast material.

On the preliminary film the authors have found calcification in mesenteric lymph nodes, peritoneal granulations, or occasionally in the tubes. Various deformities of the contrast image are seen. There may

be irregularity in the outline of the uterine canal. Filling defects may be noted along the uterine wall, and one tube may be completely blocked. The margin of the uterine shadow may be serrated or undulating, or retraction due to synechial areas may be seen. The changes in the tubes reflect the various types of pathologic change. Absence of filling, narrow areas, abnormal folds and nodular saccules may be demonstrated.

Uterotubal tuberculosis may yield to antibiotic therapy to the extent that future pregnancy occurs. Surgical and other forms of therapy are also discussed.

ÉTUDE RADIO-ANATOMIQUE DE L'OS TEMPORAL. By M. JUSTER, Chargé de Recherches au C.N.R.S., and H. FISCHGOLD, Electroradiologists des Hôpitaux de Paris, with the technical collaboration of G. KORACH. A volume of 106 pages, with 51 figures. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris 6e, 1955. Price 2,000 fr. (paper bound), 2,800 fr. (cloth).

In this work, an anatomist and radiologist have collaborated, with the idea of familiarizing specialists in different fields with the interpretation of roentgenograms of the temporal bone.

For the study, dried temporal bones were cut into sections 3 mm. thick along the axes and planes of three standard projections of radio-otology, corresponding to the views of Stenvers, Schüller, and Hirtz. Thus there were obtained vertical sections parallel and perpendicular to the major axis of the bone and horizontal sections parallel to the major axis. Radiographic enlargements, twice the actual size, were made with a focal spot of 0.3 mm. to correspond with the usual size of sections as shown in most textbooks of anatomy.

The section method presents the inconvenience of cutting such well defined structures as the cochlea, semicircular canals, etc., into several fragments. For this reason special anatomic preparations were made of the internal ear as a whole, the internal ear and the facial canal, and the auditory ossicles.

The final section of the book is devoted to a succinct description of the principal formations of the temporal bone, such as the external auditory canal, tympanic cavity, internal ear, internal auditory canal, facial canal, carotid canal, and temporal sutures.

In Memoriam

ARTHUR CARLISLE CHRISTIE, M.D., F.A.C.P., F.A.C.R.

1879–1956

The death of Dr. Arthur C. Christie on June 22 brought to a close a notable career in radiology covering some forty years and exerting an incalculable influence upon that specialty.

Arthur Carlisle Christie was born in West Sunbury, Penna., Dec. 29, 1879, the son of Dr. Milton H. Christie and Harriet Rhodes Christie. The son of a practicing physician in a rural area, he was associated with medicine throughout his life. His early education was in the public schools of Corry, Penna. He was granted his degree of Doctor of Medicine in 1904 by the Cleveland College of Physicians and Surgeons (now incorporated in Western Reserve University Medical School).

For a brief period, Dr. Christie practiced medicine in Clymer, N. Y. Leaving his general practice, he attended the Army Medical School in Washington, D. C., and was graduated as a First Lieutenant in 1907. He served on active duty in the Philippines and at various posts in the United States and, while on service at Columbus Barracks, Columbus, Ohio, became interested in radiology. Ordered to the Army Medical School as Professor of Roentgenology and Operative Surgery, he served in that capacity from 1912 to 1916. Thus starting in the infancy of a new specialty, Dr. Christie devoted his medical life to radiology. One of the earliest contributions to radiological literature in English was his *Manual of X-ray Technic* published in 1913.

In 1916 Dr. Christie resigned his commission and became associated with Dr. Thomas A. Groover in the practice of radiology in Washington, D. C. In the following year, he was commissioned a Major in the Medical Reserve Corps. Appointed Chief of the Division of Roentgenology of the Medical Department, U. S. Army, he organized this Division entirely from Reserve personnel, an outstanding achievement. He was commissioned Colonel in 1918 and served as Senior Consultant in Roentgenology, A.E.F., France, from October 1918 to February 1919.

After the First World War, Dr. Christie returned to his civilian practice with Dr. Groover, and in 1919 Dr. E. A. Merritt became associated with the two.

With his Professorship of Roentgenology at the Army Medical School in 1912, Dr. Christie began his teaching career. He was later Professor of Roentgenology at George Washington University School of Medicine and Professor of Clinical Radiology at Georgetown University Medical School. He contributed freely of his time as teacher, consultant, and adviser and, because of his warm, kindly, and thoughtful nature, old and young looked to him for advice concerning their personal careers and problems.

Dr. Christie was closely associated with almost all phases of the development of radiology from 1912 to the very end of his career. This is well attested by

Blackstone Studios, New York

Arthur Carlisle Christie, M.D.

his enormous bibliography. Besides writing extensively, he devoted much time to lectures and conferences on numerous medical and medicosocial subjects. He held membership in many medical organizations and served frequently on their official boards. He was a past President of the Medical Society of the District of Columbia; Fellow of the American Medical Association and of the American College of Physicians; past President of the American Roentgen Ray Society; member of the Radiological Society of North America; Fellow and past President of the American College of Radiology, which he helped to organize, and a recipient of its Gold Medal.

From 1924 to 1929 Dr. Christie was Editor of the *American Journal of Roentgenology and Radium Therapy*. In 1937 he was the President of the Fifth International Congress of Radiology and through that office formed many friendships with radiologists of all countries, friendships which persisted through the years. He was made an Honorary Fellow of the Faculty of Radiologists of Great Britain and was elected to honorary membership by most of the leading radiological societies of the world.

Nationally and internationally known and honored as a radiologist, Doctor Christie always stressed the fact that the specialist must be first, last, and always a physician, with all that this means in the broadest and best sense.

Dr. Christie was an ardent churchman, giving of his talents to Church, Sunday School, and the Y.M.C.A. He was for some years President of the Board of Trustees of the American University (Washington) and recently gave many lectures before civic groups. His talk on the Constitution of the United States, "Faith of Our Fathers," is widely known.

Arthur Carlisle Christie had a capacity for friendship that was unique, a deep faith in the progress of medicine and science and, above all, in humanity. He was courageous in his fight for what he believed to be right in his profession, his religion, and in society. Those who knew him best will feel his loss most deeply, but a host of others will honor and respect his memory.

FRED O. COE, M.D.

DR. GUSTAV HERRNHEISER

1890–1956

Dr. Gustav Herrnheiser, well known for his contributions to radiology, died in London, May 13, 1956. He was born and raised in Prague and took most of his training in roentgen diagnosis with Guido Holzknecht in Vienna. Having early acquired a leading position among the radiologists of the Czechoslovakian Republic, he became Professor of Radiology of the German University of Prague. Out of his broad interests, his comparative roentgen-anatomic studies of the vascular and bronchial trees of the lung, pursued through many years, and their most recent off-shoot, the study on acute pulmonary edema, stand out as contributions of permanent significance.

Dr. Herrnheiser left his beloved Prague after the Munich crisis and went first to Palestine, where he became Chief Radiologist to the Hadassah Hospital in Tel Aviv. In 1942 he moved to Alexandria, Egypt, to accept the position of Chief Radiologist at the King Fuad Hospital. After a long odyssey he "returned" to England in 1948 and was consultant radiologist to Connaught Hospital, London, and St. Margarete Hospital, Epping, in addition to conducting his office on Harley Street.

In his days in Prague, Dr. Herrnheiser was an enthusiastic teacher and many radiologists throughout the world, received their basic training or later inspiration from him. He was loved as a man and friend for his vigor and nobility. He is survived by his wife, Vera, and two daughters.

FELIX G. FLEISCHNER, M.D.

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American Radiology—1905 to 1955. Paul C. Swenson. Internat. Abst. Surg. **101:** 313–325, October 1955.

This discussion of American radiology from 1905 to 1955 is published as a collective review. In addition to his account of the advances in diagnostic and therapeutic radiology, the author includes sections on radiation physics, the teaching of radiology, and radiologic organizations and literature.

THE HEAD AND NECK

The Application of Urografin to Cerebral Angiography. W. Grote and W. Bettag. Fortschr. a. d. Geb. d. Röntgenstrahlen **83:** 579–583, October 1955. (In German)

Urografin (Schering) is a new aqueous iodine solution which has been used primarily for excretory urography. Favorable results have also been reported with this medium in cerebral angiography. The same subjective phenomena—heat and pain on the injected side and transient paresthesias—are noted as with other iodine solutions, but there have been no allergic reactions or other side-effects.

In order to obtain comparative results the authors injected Perabrodil and Urografin in the same patient, under the same circumstances. Urografin was found to produce superior contrast and more complete filling of the smaller cerebral vessels.

Five roentgenograms.

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Porencephaly. Melvin G. Alper and Joseph Dessoff. Arch. Ophth. **54:** 541–547, October 1955.

The authors review the literature on porencephaly and report a case in a twelve-year-old boy with severe right frontal headache, visual hallucinations, and homonymous hemianopsia. A history of convulsive attacks was obtained. The diagnosis was made by pneumoencephalography, which demonstrated a large porencephalic cyst, approximately 8 cm. in diameter, in the right posterior parietal area, in communication with the posterior portion of the body of the right lateral ventricle. The cyst depressed the occipital and temporal segments of the right lateral ventricle.

It is pointed out that a porencephalic cyst must be considered in the differential diagnosis of any intracranial mass lesion and that a preoperative diagnosis can be made only by pneumoencephalography or ventriculography. Because operative intervention for this condition is contraindicated as long as the cyst communicates freely with the ventricular system and subarachnoid space, the treatment is aimed at controlling the jacksonian convulsions by anti-epileptic drugs. In the case reported, the patient became symptom-free but the prognosis remains uncertain.

Three pneumoencephalograms; 1 electroencephalogram; 3 diagrams.

The Glomus Jugulare Tumour. Clinical and Radiological Features. R. S. Hooper. J. Fac. Radiologists **7:** 77–89, October 1955.

The clinical courses and radiographic and angiographic features of 5 patients with glomus jugulare tumors are presented. These tumors originate in the basal portions of the temporal bone and by their expansion erode the adjacent bone, destroying the internal ear and involving, also, the middle ear, the tympanic membrane, and not infrequently the posterior wall of the external meatus. In the latter situation the tumor may present as a vascular polyp, from which profuse hemorrhage may occur spontaneously or following attempts at removal. Below the petrous bone, the continued growth may expand the margins of the jugular foramen, compress and destroy the lower cranial nerves, and obstruct or involve the internal jugular vein or sigmoid sinus, which may fill with tumor tissue. Occasionally masses of tumor tissue may form in the neck contiguous with the tumor of the temporal bone. After a period, sometimes of years, encroachment upon the intracranial cavity takes place, papilledema occurs, and cerebellar signs may appear, before evidence of frank medullary compression becomes manifest.

Radiologic demonstration of involvement of the temporal bone is an important factor in establishing the diagnosis and assessing the progress of the condition. Routine roentgenograms of the skull show: (1) sclerosing or blurring of the tail of the mastoid region, which, however, is indistinguishable from that seen in chronic infection of the mastoid; (2) enlargement of the jugular foramen, ranging from simple expansion of the foramen by the tumor to widespread erosion of adjacent bone; (3) erosion of the petrous portion of the temporal bone, usually detectable in a standard anteroposterior projection, though other views may make it more evident. The radiologic change produced by acoustic neuroma is occasionally similar to the appearance which is considered typical of the glomus jugulare tumor, but the erosion caused by neuroma is usually confined to the internal auditory meatus and is seen as a widening of the canal.

Angiograms of the external carotid artery and its branches of distribution were found most helpful in diagnosis. The following characteristic changes were observed in the angiograms obtained: (1) an increase in number and size of the branches of the external carotid artery passing through the region of the temporal bone; (2) greatly increased density of the temporal bone as the contrast material passes through; (3) the appearance of small vascular channels or loops around the fringe of the shadow of the temporal bone; (4) the presence of direct or indirect arteriovenous anastomosis; (5) evidence of obstruction of the lateral or sigmoid sinus and reversal of flow in this venous channel.

The management of this condition is discussed in the light of the radiographic evidence provided in the clinical course of the tumor. The author lists the following guiding principles: "(1) External carotid arteriograms have been obtained. If the characteristic appearance is seen the diagnosis is made certain. (2) The external carotid artery is ligated after the completion of the angiograms, to diminish the blood supply to the tumor. When a bruit is present this stops or greatly reduces the noise. (3) If papilledema or other phenomena suggest much encroachment upon the posterior fossa, a suboccipital decompression is performed. (4) The patient is later subjected to courses of deep x-ray therapy."

Eight roentgenograms; 2 drawings.

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THE CHEST

Bronchography by the Aspiration of Contrast Media. Björn Nordenström. Acta radiol. **44:** 281–288, October 1955.

In bronchiectasis there are often diffuse changes in the bronchi, the extent of which cannot be determined on ordinary roentgen films or tomograms. Bronchographic exploration of the bronchial tree is therefore indispensable; it calls, however, for *complete* examination of all bronchial ramifications. If the examination is incomplete, the patient may not be radically cured in spite of surgical intervention.

In the author's bronchographic technic, the patient himself aspirates the contrast substance. The pharynx is anesthetized with 2 per cent tetracaine administered by spraying. For the trachea and bronchial tree of the lung to be studied, 3 to 6 ml. of tetracaine is instilled between the vocal cords with a laryngeal syringe. When the patient's position is altered, the fluid is directed to the various ramifications of the bronchial system.

The contrast medium (Dionosil) is injected through a radiopaque sterilized plastic catheter, 48 cm. in length, into the main bronchus of the lung to be examined, a few centimeters below the carina, in expiration. The patient is then asked to take a deep inspiration, so as to aspirate the medium. The contrast filling of the bronchi is controlled fluoroscopically.

With this procedure, the author has obtained excellent bronchograms. In order for the contrast medium to be aspirated, however, the bronchi must retain some of their normal aerating capacity. In cases of bronchiectasis, they often contain secretion, with consequent atelectasis. Therefore, careful draining and drying of the bronchi before examination is of special importance. This technic may be supplemented by selective bronchography if necessary.

A bronchus should not be considered free from ectatic changes until it has been proved so by contrast filling. One of the most valuable results of this technic is the excellent representation of the bronchial mucosa.

The author has encountered no complications in connection with this method; it has proved useful in the bronchographic examination of patients suffering not only from bronchiectasis, but also with pulmonary tuberculosis and neoplasms.

Six roentgenograms; 1 photograph.

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Bronchography with Dionosil. G. H. C. Joynt and L. R. Harnick. Surg., Gynec. & Obst. **101:** 425–430, October 1955.

Dionosil is an aqueous suspension of a radiopaque substance of low solubility, differing fundamentally from the oily iodides or aqueous solutions. An oily suspension is also available. The aqueous suspension is 50 per cent weight per volume of propyliodone, with the addition of sodium carboxymethyl cellulose. Sodium citrate is present as a buffer, and the preparation is rendered isotonic with sodium chloride. Some benzyl alcohol is used as a bacteriostatic agent. Dionosil Oily is a 50 per cent weight per volume suspension of the same substance in pure arachis oil.

The most important advantage of Dionosil is its rapid elimination from the lungs in three or four days. It appears to be well tolerated by the patient, although occasionally there is a febrile reaction lasting for twenty-four to forty-eight hours.

The authors studied the effect of Dionosil and Dionosil Oily after introduction into the bronchi in dogs. No granulomatous reaction with the aqueous suspension was noted in the lungs after four weeks. With Dionosil Oily, there was some patchy atelectasis and granulomatous reaction and there appeared to be a greater tendency to alveolar filling. The oily suspension offers the advantage of being somewhat less irritating to the mucous membrane, but with good topical anesthesia there has been little discomfort from the aqueous preparation.

Six roentgenograms; 5 photomicrographs; 2 tables.

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Propyliodon-Cilag-Suspension, a New Contrast Medium for Bronchography. W. Bessler. Fortschr. a. d. Geb. d. Röntgenstrahlen **83:** 553–559, October 1955. (In German)

Propyliodon (Cilag), an Isotonic Aqueous Contrast Medium for Bronchography. H. J. Gombert and R. Hoffmann. Fortschr. a. d. Geb. d. Röntgenstrahlen **83:** 559–562, October 1955. (In German)

Aqueous iodine solutions for bronchography have so far been unsatisfactory. Being hypertonic, they cause irritation of the bronchial mucosa, and large doses of anesthetics are necessary, up to full tolerance. Nevertheless, the roentgenologist has to act quickly to complete his examination. Otherwise, coughing and expectoration will interrupt the study prematurely.

Propyliodon, a new aqueous solution for bronchography, is an improved Dionosil, containing 28.4 per cent iodine. It is an isotonic solution, causing less irritation than other media and requiring less anesthesia of the bronchial mucosa. It mixes well with the secretions and results in a complete filling of the bronchial lumen instead of the thin coating formerly obtained. After expectoration, a thin layer of the medium may remain, but this is absorbed within forty-eight hours.

Bessler reports the use of Propyliodon in 100 consecutive cases. In 95 per cent there was complete visualization of all branches of bronchial segments. Allergic reactions were not observed.

Gombert and Hoffmann used Propyliodon in 30 consecutive cases and report that the results were gratifying, especially since the medium was well tolerated and produced no side-effects. These authors also found that Propyliodon caused less irritation than other, more viscous aqueous contrast solutions and that less local anesthesia was therefore required. Preheating of the medium was not necessary. It is absorbed at a much slower rate than other water-soluble media, and traces were sometimes visualized after one or two days. When Propyliodon is not completely expectorated at once, a relief picture of the bronchial tree can be obtained, which is a distinct advantage.

Both of these papers include roentgenograms (Bessler, 4; Gombert and Hoffmann, 3).

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Newington, Conn.

Congenital Intra-Lobar Sequestration of the Lung. Report on Four Cases. Denis N. Fuller. South African M. J. **29:** 987–992, Oct. 15, 1955.

Four cases of congenital intralobar sequestration of the lung are presented, in each of which x-ray study,

with or without bronchography, aided in the diagnosis. While the sequestrum may consist of one large cyst, it is more frequently multiloculated or composed of a system of branching bronchi, widely dilated and filled with mucus.

The embryologic theory currently considered most tenable is that the developing lung bud receives its blood supply from the primitive dorsal aorta rather than from the ventral aorta. The lung bud subsequently becomes "captured" by its blood supply and grows independently, detaching itself from the normally connected bronchopulmonary system.

Roentgen study reveals an area of opacity or air-containing cyst, sometimes with a fluid level, situated paravertebrally in the costophrenic sinus. Bronchography demonstrates a space-occupying mass which displaces and possibly replaces the normal bronchi. Bronchiectasis of the normally connected lobe may be associated. Some of the contrast medium may gain access to the cyst itself but, because of the gelatinous nature of the cyst contents, all that is apparent may be a series of opaque globules within the mass. It is suggested that a barium swallow should always be undertaken to demonstrate possible esophageal abnormality or hiatus hernia.

Surgical excision is the only treatment.

Eight roentgenograms.

Transitory Exacerbation of Fever and Roentgenographic Findings During Treatment of Tuberculosis in Children. C. B. Choremis, C. Padiatellis, D. Zoumboulakis, and D. Yannakos. Am. Rev. Tuberc. **72:** 527–536, October 1955.

The return of fever and an increase in roentgen signs of disease was observed in 22 of 43 children treated for primary tuberculosis with isoniazid and streptomycin. Since clinical study showed no allergic phenomena and no secondary infection, the findings were felt to be on the basis of liberation of tuberculin in large amounts, as a result of marked bacteriolysis. The fever was associated with increased physical findings, as well as an aggravation of the roentgenographic findings. The changes on the chest film consisted of atelectasis or an increase in infiltrative disease, usually in the parahilar region on the involved side. These changes regressed slowly, with definite improvement usually apparent in a month. There was no decrease or cessation of drug therapy during the episodes.

Seven cases are reported in detail, with roentgenograms showing the changes during the febrile episode. The authors suggest that cortisone might be used during this transitory phase to modify the exudative changes or to prevent them.

Ten roentgenograms; 7 temperature charts.

JOHN H. JUHL, M.D.
University of Wisconsin

On the Prognosis of Childhood Tuberculosis. An Eighteen-Year Follow-Up Report. Nils Levin. Am. Rev. Tuberc. **72:** 513–526, October 1955.

In 1935 the author published the results of a roentgenologic and bacteriologic study of 434 children up to the age of fifteen years with suspected or verified active tuberculosis (Acta paediat., supp. 1, **17:** 160–169, 1935). This group has now been followed for an average of eighteen years (sixteen to twenty-two years). Of 379 survivors, all but 18 consented to re-examination by standard or mass roentgenography. They were then classified into the following groups on the basis of roentgenographic findings: 1. No demonstrable lesions. 2. Calcification, either in the pulmonary parenchyma or in hilar nodes. 3. Inactive tuberculosis, in which roentgenographic study revealed parenchymal lesions of quiescent appearance (occasionally checked by culture of gastric washings). 4. Active, with pulmonary lesions suggestive of active tuberculosis. Some evidence of healed tuberculosis was found in 33 per cent of the persons for whom gastric washings were originally negative and in 43 per cent of those who were initially positive bacteriologically.

A striking difference in the mortality rate was noted when the "primary" tuberculosis group was compared with the post-primary (adult type of tuberculosis) group, the figures being, respectively, 7 and 63 per cent. In the primary group, the mortality increased with age at onset, while in the other group the opposite was true except for an increase at puberty.

There were 34 deaths due to tuberculosis, 26 from pulmonary disease and 8 from tuberculous meningitis in the series. Meningitic deaths were more common in the primary than in the adult type of the disease. In both groups, most of the deaths from this cause occurred in early childhood.

One chart; 10 tables.

JOHN H. JUHL, M.D.
University of Wisconsin

A Mass Miniature X-Ray and Tuberculin Survey in the Orange Free State and Northern Cape. H. Dubovsky. South African M. J. **29:** 992–997, Oct. 15, 1955.

The results of a mass miniature x-ray and tuberculin survey in the Orange Free State and Northern Cape, South Africa, are reported. The survey was begun in November 1953 and was completed in March 1954; the total number of films studied was 19,886, the number of tuberculin tests, 7,289. A 70-mm. film was used, the unit being operated at an average rate of 100 persons an hour, with 600 as a daily average. The sample material, obtained on the basis of voluntary presentation for examination, was found to have a randomness for age and sex distribution in keeping with the true demographic state. Except for deficiencies attributable to slight over-reading, 70-mm. film was found to be at least as effective as others.

In determination of prevalence rates only miniature films with a typical appearance of re-infection (adult) type of tuberculosis and the progressive primary types were used. The sites and character of opacities were guides in this selection.

The roentgen findings are summarized in tabular form; the highest prevalence rate was noted in Native reserves of the Northern Cape. A tendency to increasing prevalence as the survey moved from the city to rural areas is in contradistinction to a trend noted in a survey twelve years earlier.

Four histograms; 1 graph; 2 tables.

Pulmonary Alveolar Microlithiasis, or Calcinosis of the Lungs. Theodore L. Badger, Leonard Gottlieb, and Edward A. Gaensler. New England J. Med. **253:** 709–715, Oct. 27, 1955.

The authors describe an interesting but rare syndrome in which small laminated concretions are deposited within the alveolar spaces. The case reported is believed to be the third in English and the eleventh in the world literature. Long before symptoms appear,

the roentgenogram shows startling changes: a ground-glass mottling, spreading out symmetrically from the hili into the mid-lung fields, sparing the apices and bases until late in the course of the disease. With progression of the lithiasis, the remaining relatively uninvolved lung shows emphysematous blebs and bullae.

The authors' patient died about ten years after discovery of the condition on a routine x-ray examination of the chest. At necropsy the combined weight of the lungs was 3,300 gm.; they stood erect when removed from the chest cage, and cut with great difficulty. Multiple minute calcific concretions were scattered on the surface and were found lying in the alveoli. The less involved spaces showed these tiny stones lying free, the thin alveolar walls showing no signs of a foreign-body reaction. In the more heavily involved areas of the mid-lung fields there was giant-cell reaction encircling the microliths and blending of the alveolar wall with interalveolar fibrous tissue.

For the last eighteen months of the patient's life, in which dyspnea became increasingly unbearable, multiple urinary calculi consisting of calcium oxalate were passed. Stones were seen within the kidneys roentgenologically and at autopsy.

As pointed out by Wells (Arch. Int. Med. **7**: 721, 1911), the most tenable explanation of this precipitation of calcium in otherwise normal lung, kidney, and stomach (the latter not seen in this case) is the relative alkalinity of the parenchymal tissue of the organ following the liberation of acid (CO^2 in the lungs; HCl in the stomach; acid sodium phosphate in the kidneys). The calcium salts are less soluble in the relatively alkaline blood and parenchyma, leading to their precipitation. Some constitutional predilection must, however, be present, since these changes are so rare and physiological changes in pH so universal.

Three roentgenograms; 2 photographs; 2 photomicrographs; 2 tables.

SAUL SCHEFF, M.D.
Boston, Mass.

Roentgen Manifestations of Necrotizing Granulomatosis and Angiitis of the Lungs. Daniel Kornblum and Robert Fienberg. Am. J. Roentgenol. **74**: 587–592, October 1955.

There have recently appeared in the literature a number of reports of granulomatosis with angiitis of the lungs, usually associated with massive necrosis of the spleen and focal granulomatous glomerulonephritis. Three cases previously reported by Fienberg (Am. J. Clin. Path. **23**: 413, 1953; Am. J. Path. **29**: 913, 1953) are again recorded here, with the idea of bringing the condition to the attention of radiologists. It is characterized by the formation of aseptic circumscribed granulomatous masses in which cavity formation and necrotizing arteritis and phlebitis are seen.

Roentgenologically, the nodules or masses in the lungs are usually multiple. They are generally round, discrete and fairly well demarcated but may be confluent. Clinically the diagnosis is suggested in the presence of hemoptysis, fever, and joint pains, together with signs of glomerulonephritis.

In many instances hypersensitivity has been considered the causal factor in this disease. The course may be protracted but with the onset of glomerulonephritis, the patient's condition deteriorates rapidly.

Eight roentgenograms.

ROBERT H. LEAMING, M.D.
Memorial Center, N. Y.

Pulmonary Lesions in "Rheumatoid Disease" with Remarks on Diffuse Interstitial Pulmonary Fibrosis. Eli H. Rubin. Am. J. Med. **19**: 569–582, October 1955.

With increasing use of routine chest roentgenography, changes are being discovered in the lungs of patients with "rheumatoid disease" indicating that these organs are involved quite frequently and early in the course of the illness. Within a space of two months the author observed 3 patients with acute "rheumatoid disease" with characteristic articular manifestations in whom the chest x-ray findings were in keeping with a systemic disturbance.

A review of the cases reported in the literature and of those recorded in this article brings out a number of clinical features which, in addition to the pathologic changes previously described, would indicate that the pulmonary and joint lesions of "rheumatoid disease" are part of the same disturbance. The histories of many of the patients point to an allergic background. In the vast majority, the joint symptoms antedated the pulmonary manifestations. In a few, the pulmonary symptoms appeared at the time of recrudescence of joint symptoms. On rare occasions, acute joint and pulmonary manifestations appeared simultaneously at the onset of the disease.

At times the pulmonary infiltrations are transitory. The most frequent expression of the disease in the chest is a pleuritis manifesting itself in small serous effusions; large collections of fluid are more apt to be associated with anasarca than to be caused by cardiac failure. A pleural friction rub is often heard on auscultation. Roentgenograms of the chest usually show a bilateral, more or less symmetrical distribution of abnormal lung markings. Occasionally, solitary and nodular lesions are seen. The bilateral pulmonary mottlings frequently seen roentgenologically in "rheumatoid disease" represent interstitial parenchymal changes related to the underlying disease. The infiltrations are small and evenly distributed, simulating miliary tuberculosis, or of a nodular character, affecting chiefly the mid and lower lung fields and resembling sarcoidosis, inhalation dust disease, or bronchogenic tuberculosis, or they may be irregular and of patchy distribution, as in viral or bacterial bronchopneumonia. After subsidence of the acute phase of the disease, the markings assume a more linear configuration, forming a delicate or coarse reticular network such as is seen in lymphangitic carcinomatosis or diffuse interstitial fibrosis of the lungs. In long standing disease secondary bronchopneumonia and suppuration tend to obscure the basic pattern.

Eight roentgenograms; 2 photomicrographs.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

Obstructive Emphysema in Pneumonia Simulating Cavity. Gordon L. Snider and David B. Radner. Dis. of Chest **28**: 439–446, October 1955.

Ring shadows are described in the chest films of two adult male patients with pneumonia. These shadows occurred in the upper lobe following a history of acute lower respiratory infection of several weeks duration. Tuberculosis and lung abscess were considered. In each instance an earlier normal chest film was available for comparison. The patients were followed for several months before complete clearing of the lesions was observed.

The findings are explained as pseudocysts, produced

by check-valve formation secondary to inflammatory involvement of the bronchial mucosa with congestion and edema. Such findings in children, because of the narrower airways, are not unusual. In elderly patients they can be related to decreased effectiveness of coughing.

To be differentiated are non-putrid lung abscess and cavity formation in a bland pulmonary infarct. Neoplasms and tuberculosis must, of course, be considered.

Eight roentgenograms.

DONALD DEF. BAUER, M.D.
Coos Bay, Ore.

Anatomic and Clinical Study of Bronchial Lesions in Sarcoidosis of B. B. S. P. Marland and Y. Rose. J. franç. méd. et chir. thorac. **9:** 530–540, 1955. (In French)

Previous studies in endothoracic sarcoidosis (Besnier-Boeck-Schaumann) have been devoted largely to mediastinal lymph node and interstitial pulmonary parenchymal manifestations. More recently, bronchial lesions have been demonstrated to be of importance. Involvement of the bronchi may be the result of extrinsic compression by enlarged lymph nodes or peribronchial or endobronchial infiltrations, leading to bronchial or bronchiolar stenosis and bronchiectasis.

Specific bronchial alterations, to which are often added a cicatricial sclerosis, vascular, and probably nervous lesions, lead to stenosis and dilatation, which in turn may produce obstructive emphysema, partial atelectasis and retention and superinfection of secretions.

Bronchial involvement in sarcoidosis gives rise to three types of radiographic images: homogeneous infiltrates of lobar or segmental topography, plaques surrounded by radiolucent zones, and dense perihilar sclerotic zones. Bronchoscopy and biopsy of the bronchial mucosa may reveal some of the lesions. Bronchography aids in delineating stenotic and dilated bronchi unsuspected on plain films and at bronchoscopy.

The bronchial granulomas may heal spontaneously or lead to formation of chronic stenosis and dilatation of bronchial segments. ACTH and cortisone often produce improvement.

CHARLES M. NICE, JR., M.D.
University of Minnesota

Non-tuberculous Tracheobronchial Adenopathy. Emilio Alemán. Rev. pediat. cubana **27:** 575–588, October 1955. (In Spanish)

The author presents 7 cases of non-tuberculous mediastinal lymphadenitis in children, with parenchymal or pleural involvement in some. There was no history of contamination in any instance, and the tuberculin test was negative in the 1:10 dilution. Standard roentgenograms, planigrams, and bronchoscopy were valuable aids in diagnosis. All of the lesions healed spontaneously without sequelae, with regression of the abnormal radiologic shadows in three to nine months.

The importance of differentiating these cases from tuberculous lymphadenitis is stressed.

JAMES T. CASE, M.D.
Santa Barbara, Calif.

Sternal Metastases and Their Mechanism of Production. Carlos Gil y Gil. Am. J. Roentgenol. **74:** 609–614, October 1955.

Sternal contamination from tumors of the mammary gland may occur by either of two routes: by way of the veins or by way of the lymph stream.

The entry of the neoplastic cells into the mammary veins takes place by corrosion of the venous walls by the tumor, and is believed to be due to the proteolytic action of the neoplastic cells. From these veins the accumulation of tumor cells or the neoplastic thrombus comes to rest in the intercostal veins. From this location the tumor cells have two pathways by which to spread. They may be directed anteriorly and empty directly into the sternum, or they may reach this bone through the internal mammary veins. If, on the other hand, the malignant cells are directed toward the posterior aspect of the thorax, they may reach the prevertebral venous plexuses and contaminate the vertebrae, the pelvis, and the cranium.

Proof of sternal seeding may be accomplished in three ways: (1) by the Gil y Gil sign (localized or diffuse pain on pressure of the finger tip against the surface of the sternum); (2) by sternal roentgenography; (3) by sternal puncture.

Lymphatic contamination may occur by way of the lymphatics from the breast and by the deep lymphatics of the thoracic wall to the retrosternal nodes. Metastases in the internal mammary chain may grow to such an extent as to rupture the capsule, producing propagation of the tumor *in situ* if the involved node is attached to the posterior aspect of the sternum. The proteolytic property of the neoplastic cells causes destruction of the periosteum of the compacta of the posterior sternal wall. This amounts to neoplastic extension *per contiguitatem*.

The existence of a possible direct lymphatic pathway between the breast and the spongiosa of the sternum has not yet been observed by the author, but its presence is suspected.

Six roentgenograms.

J. F. MARTIN, M.D.
Bowman Gray School of Medicine

THE CARDIOVASCULAR SYSTEM

Patent Ductus Arteriosus. Some Notes on Prognosis and on Pulmonary Hypertension. Maurice Campbell. Brit. Heart J. **17:** 511–533, October 1955.

Experiences with 160 cases of patent ductus arteriosus (including 20 in patients past thirty-five years of age) are here reviewed to determine if surgery is always indicated and, if so, when. The article should be read in the original by anyone really interested in the subject, since only the conclusions can be given in the space of an abstract.

Although a few patients will reach fifty or sixty years of age with a minimum of disabling symptoms and in still fewer the ductus will close spontaneously, the author believes that the risk of surgery is small enough and the benefits great enough to warrant it in every case where it is feasible. He makes a few exceptions: those in whom the ductus appears to be closing spontaneously, those in whom the shunt is very small and causing no strain, and older patients with pulmonary hypertension and a reversed shunt. He believes that this last group could be operated upon successfully if diagnosis were made early enough, before the occurrence of irreversible changes in the pulmonary arteries.

Nine roentgenograms; 6 electrocardiograms; 2 photographs; 7 tables.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

The Diagnosis of Tricuspid Stenosis. Ronald Gibson and Paul Wood. Brit. Heart J. **17:** 552–562, October 1955.

The authors present a study of 14 cases of rheumatic tricuspid stenosis. Nine of the group were from a series of 300 cases of mitral valve disease previously reported by Wood (Brit. M. J. **1:** 1113, 1954. Abst. in Radiology **64:** 447, 1955). In all but 3 of the 14 cases, mitral stenosis was the predominant lesion. A case of isolated tricuspid stenosis associated with disseminated lupus erythematosus is also reported.

The most characteristic radiologic finding in this group of cases was conspicuous dilatation of the right atrium without pulmonary artery enlargement and with relatively little pulmonary venous congestion. In no instance was calcification demonstrable in the tricuspid valve.

Clinical features were high venous pressure, giant "*a*" waves in the jugular phlebogram, electrocardiographic evidence of right atrial hypertrophy, and a diastolic or presystolic tricuspid murmur.

Cardiac catheterization established the diagnosis by showing a presystolic or diastolic pressure gradient across the damaged valve, averaging 6 mm. Hg. The diagnosis was made first by this method in 3 instances; in the others by clinical and roentgenographic studies.

Eleven figures, including 2 roentgenograms; 1 table.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Ebstein's Anomaly of the Tricuspid Valve: Angiocardiographic Diagnosis. Albert D. Kistin, John M. Evans, and Alfred E. Brigulio. Am. Heart J. **50:** 634–640, October 1955.

In Ebstein's anomaly the tricuspid valve is displaced to an abnormally low position, so that the volume of the right ventricle becomes reduced. Angiocardiograms in these cases show distinctive characteristics, as follows: enlargement of the right auricle and rapid opacification of the entire heart shadow, leaving a thin wall of right ventricle on the left heart border; the presence of a notch, seen in systole, on the inferior border of the opacified right heart, identifying the position of the valve; abnormal persistence of opacification of the right atrium and ventricle; poor visualization of the pulmonary arteries, left heart, and aorta, except in the presence of a right-to-left shunt.

The authors report one case which showed cardiac enlargement on the plain chest film, with a rounded prominence above the apex suggestive of ventricular aneurysm. Angiocardiograms clearly demonstrated the division of the right ventricle into a proximal atrialized portion and a distal functioning portion by the notching mentioned above.

Tetralogy of Fallot, pulmonary stenosis, and tricuspid atresia need to be considered in differential diagnosis.

Four roentgenograms; 3 drawings; 1 electrocardiogram.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Combined Ventricular Septal Defect and Aortic Insufficiency. Jan Philipson and Georg-Fredrik Saltzman. Acta radiol. **44:** 269–280, October 1955.

The authors review briefly 7 previously described cases of combined ventricular septal defect and aortic insufficiency and report 4 cases of their own. In addition, a description is given of 2 cases similar from the hemodynamic aspect but without sufficiently extensive examinations to "clear up all the details." One of the 4 cases was proved by autopsy. In the others the diagnosis was confirmed by means of blood-oxygen determinations and blood-pressure measurements carried out in conjunction with heart catheterization, as well as by thoracic aortography or selective angiocardiography. All 6 patients were men, ranging in age from fifteen to twenty-six years. All were acyanotic.

Conventional roentgenography showed the heart to be greatly enlarged in every case, varying from 700 to 1,780 c.c. per square meter of body surface. The enlargement was general; in a few cases dilatation of the left ventricle was particularly pronounced. The pulmonary artery with its branches was moderately dilated. The aorta was of normal caliber in 5 cases, and in 1 case slightly enlarged. In every instance, fluoroscopy revealed large heart pulsations which appeared to be of the same nature as those seen in aortic insufficiency. Large pulsations were also noted in the great vessels.

The authors believe that it should be possible to make a correct diagnosis of combined ventricular septal defect and aortic insufficiency in the living subject. Important signs and symptoms may be established even at the clinical examination. In an acyanotic patient with cardiac symptoms dating from earliest infancy, the combination of a palpable thrill, a systodiastolic murmur with maximum loudness over the third and fourth intercostal space, and a high pulse pressure, should suggest the presence of the defect.

The differential diagnosis from patent ductus arteriosus should be given special attention. It is usually possible to make this distinction with the help of clinical data and a conventional roentgen examination, though in a few cases cardiac catheterization may be necessary.

In the 4 cases reported in which diagnosis was confirmed, the etiology of the insufficiency could be demonstrated only in the case which was submitted to autopsy. Here it was thought to be due to an acquired defect.

Fourteen roentgenograms; 2 tables.

PAUL O'BRIEN, M.D.
Bowman Gray School of Medicine

Echinococcus Disease of the Left Ventricle. A Clinical, Radiologic and Electrocardiographic Study. Eduardo Joaquín Canabal, César V. Aguirre, Jorge Dighiero, Joaquín Purcallas, José M. Baldomir, and Carlos V. Suzacq. Circulation **12:** 520–529, October 1955.

The clinical, electrocardiographic, and radiologic features of 3 cases of echinococcus disease of the left ventricle which were diagnosed correctly, localized accurately, and operated upon successfully, are presented and discussed.

Involvement of the heart in echinococcus disease is unusual. The left ventricle appears to be the site of predilection, presumably because of its richer coronary circulation, by way of which the parasite is conveyed. Since uncomplicated cases present no particular clinical features, early recognition (before rupture) is possible only by radiography and electrocardiography.

Radiologically the hydatid cyst is recognizable, after a period of growth and host reaction, by a localized bulge in the cardiac silhouette and calcification of its wall. Angiocardiography may demonstrate localized

deformities and filling defects within the ventricular cavity. Tomography usually gives useful information as to the size, shape, and location of the intramural cyst, as well as about the outline and position of calcific zones when present. Electrocardiography will in most cases show a local area of ischemia.

Early surgical intervention is strongly recommended.

Four roentgenograms; 4 electrocardiograms.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

An Aid to Aortography. W. Barr Stirling. Proc. Roy. Soc. Med. **48:** 823–827, October 1955.

The importance of rapid delivery of the opaque material in translumbar aortography is emphasized in this paper. The author has invented a mechanical injection device for this purpose. It consists of a metal stand which holds a syringe in vertical position and on which is suspended a vertical lever. The apparatus is operated manually, a downward stroke of the lever forcing the opaque material rapidly out of the syringe and, through pressure tubing, into the needle, which has been introduced into the aorta. With this device it is possible to inject 18 c.c. of 70 per cent Urokon in not more than one second. Although this rapid injection requires pressure of the order of 800 mm. Hg through a 16 gauge S. W. G. needle, experimental studies carried out both with cadaveric specimens and on patients indicate that the use of this device is safe.

Five roentgenograms; 1 photograph.

RICHARD G. LESTER, M.D.
University of Minnesota

Lumbar Aortography in Acute Aortic Embolism. Herman Lodin. Acta radiol. **44:** 289–292, October 1955.

The clinical diagnosis of an obstruction in the lower part of the aorta and the upper part of the common iliac arteries may be established with relative certainty. Without the use of aortography, however, it cannot be determined whether the occlusion is complete, or at what level its upper limit lies. Thus, the author feels that, from the point of view of surgery, aortography is indicated in every case of acute aortic embolism. (Aortography cannot show the distal extent of the occlusion.)

Four cases in which lumbar aortography was performed for acute aortic embolism are reported. Following premedication with Pethidine, direct aortic puncture was performed in the ordinary way, with the patient in the prone position, under light NO_2-ether anesthesia. Twenty to twenty-four milliliters of Umbradil 35 per cent or 50 per cent was injected manually, and the roentgen exposure was made at the moment increased resistance was felt. Subsequently, the contrast medium was diluted in the aorta with physiologic saline, and the needle was removed. Despite the fact that all of these patients had severe cardiac disease, no difficulty was encountered in performing this procedure in the prone position. Manual injection at low pressure appeared to obviate the risk of overloading the kidneys with contrast medium, and fragmenting the embolus. The superior margin of the embolus was well demonstrated in all cases, and no complications appeared to result from the examination.

Four roentgenograms.

G. BROGDON, M.D.
Bowman Gray School of Medicine

Chronic Massive Pulmonary Artery Thrombosis. Alfred Ring and Jens R. Bakke. Ann. Int. Med. **43:** 781–806, October 1955.

Massive pulmonary embolism as a cause of sudden death is a relatively common autopsy finding. Chronic thrombosis of the main pulmonary artery or of the right or left main branches is, in contrast, of rare occurrence, and reported cases are limited in number.

In a total of 11,511 consecutive autopsies from Queens General and Triboro Hospitals (Jamaica, N. Y.), 21 cases (0.18 per cent) of massive pulmonary artery thrombosis were found. Only those cases with complete occlusion of the main pulmonary artery or the main right or left primary branches were included in the series. The premortem nature of these thromboses and their chronicity were judged by such characteristics as lines of Zahn, lamination of layers, adhesiveness to the vessel wall, and degree of organization. The right main pulmonary artery alone was involved in the process in 9 cases, and the left alone in 4 cases. Both right and left pulmonary arteries were involved in 8 patients.

Cases of massive pulmonary thrombosis may be divided into two main groups: (1) those superimposed upon a previous pulmonary embolus, and (2) those arising *in situ* without any previous embolic episode, and hence autochthonous.

In chronic heart disease, particularly with heart failure, the resultant chronic passive congestion of the lungs offers a good breeding ground for thrombosis, especially in the presence of a cor pulmonale. Autochthonous thrombi may also result from localized disease of the pulmonary arterial wall, such as congenital or syphilitic aneurysms of the pulmonary artery, acute pulmonary arteritis due to local disease of the surrounding lung or complicating ductus arteriosus, and in syphilitic arteritis.

The clinical picture of pulmonary thrombosis is often masked by the underlying and complicating lesions of the lungs or heart. This undoubtedly accounts for the difficulty in antemortem diagnosis. Dyspnea is usually the outstanding symptom and, as a rule, is severe. Cyanosis is also a prominent feature. Other symptoms which may be present include cough and thoracic or epigastric distress.

Most patients develop evidence of right heart hypertrophy with subsequent right heart failure due to cor pulmonale. This is often the mode of death.

Diagnosis is difficult. Radiographically an abnormal hilar mass due to enlargement of the pulmonary artery may be seen. In addition, as a result of the obstruction, the lung fields appear abnormally radiable, with absence of vascular markings. On fluoroscopy, absence of hilar pulsation on the involved side is noted. Angiocardiography is an excellent method for confirming the presence of pulmonary obstruction when massive thrombosis is suspected. Finally, if right heart catheterization is done, the presence of high right ventricular pressure with a low cardiac output may be found.

The continued use of anticoagulants may prevent further propagation of the clot and, in view of the dire prognosis, is worthy of a prolonged trial. The pulmonary vasculature has a tremendous reserve, and the maintenance of only a small lumen may extend life for a reasonable period.

Despite massive thrombosis, a notable absence of any massive infarction is observed. This is undoubtedly

due to the well known anastomoses between the pulmonary and bronchial arteries.

Three photographs; 1 table.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Pulmonary Arteriovenous Fistula. Angiocardiographic Observations in Nine Cases. Israel Steinberg and John McClenahan. Am. J. Med. 19: 549–568, October 1955.

Pulmonary arteriovenous fistulas are hereditary hemangiomatous malformations of the pulmonary vascular bed. In almost 40 per cent of the reported cases there also are hemangiomas elsewhere in the body, indicating a close relationship to familial hemorrhagic telangiectasis.

When pulmonary arteriovenous fistulas are large and do not have systemic arterial connections, dyspnea, cyanosis, clubbing of the digits, and polycythemia result from unsaturation of the blood. Hemoptysis may occur when there is rupture of the anomalous communication. There is also a high incidence of cerebral symptoms due either to cerebral thrombosis, secondary to the polycythemia, or to infection, especially brain abscess. The heart remains normal in size because pulmonary arteriovenous fistulas do not cause increased pulmonary vascular resistance.

Nine cases are reported, in only 1 of which was the classical syndrome of cyanosis, clubbing, polycythemia, and murmur present. In 1 patient chronic anemia prevented intense cyanosis and polycythemia. In 3 instances the patients were asymptomatic; in 2, the pulmonary arteriovenous fistula was an incidental finding; in the remaining 2, brain abscess and meningoencephalitis caused the presenting symptoms. Vascular bruits were heard in 8 patients.

The diagnosis of pulmonary arteriovenous fistula can often be made by conventional roentgenography. Pulmonary densities with hilar vascular connections localized in lobes or segments of the lung, or increased hilar vascularities, should arouse the suspicion of an arteriovenous fistula. Change in size of the lesions after the Valsalva or Müller maneuver and delineation of the afferent arterial and efferent venous connections by body-section radiography may be confirmatory. Angiocardiography establishes the diagnosis and is recommended for preoperative evaluation.

Twenty-seven roentgenograms; 4 photographs; 1 drawing; 1 table.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

Treatment of Aneurysm of the Hepatic Artery by Excision. Report of Case. John W. Kirklin, Everett Shocket, Mandred W. Comfort, and Kenneth A. Huizenga. Ann. Surg. **142**: 110–114, July 1955.

The authors report a case of aneurysm of the hepatic artery in a 52-year-old female, which was unique in two respects: The diagnosis was established preoperatively by aortography, and the aneurysm was successfully excised.

The patient had experienced attacks of abdominal cramps since 1944. Roentgenograms of the gallbladder and stomach and an electrocardiogram were reported to be normal in 1947. In 1954, severe back pain and hematemesis resulted in hospitalization, at which time 2 films of the gallbladder failed to show any concentration of contrast medium in the subhepatic area; neither was any abnormality disclosed in 2 roentgenograms of stomach and 1 of the colon. Persistent bleeding led to laparotomy and the discovery of a large pulsating tumor just below the diaphragm, believed to be an aneurysm. It was aspirated, but hematemesis recurred. An aortogram was then made by percutaneous injection into the thoracic aorta of 20 c.c. of 70 per cent Urokon Sodium, under anesthesia. A saccular accumulation was readily detectable just lateral to the area of the celiac axis; this was interpreted as an aneurysm of a main branch of the celiac artery. At operation the lesion was found to involve the hepatic artery. The postoperative course was favorable.

One roentgenogram; 2 drawings.

THE DIGESTIVE SYSTEM

Congenital Anomalies of the Esophagus. J. S. Battersby. Arch. Surg. **71**: 560–568, October 1955.

None of the congenital anomalies offer a greater challenge than those of the esophagus. Diagnosis must be made earlier; surgical treatment must be improved; and preoperative and postoperative care must be better managed if the high mortality is to be reduced.

This paper is a review of 90 cases of congenital lesions of the esophagus seen over a sixteen-year period. These are divided into two groups: one (13 per cent) consisting of duplication, stenosis, cardiospasm, and atresia without fistula; the other (87 per cent), of tracheal esophageal fistulas and atresias with fistula. Associated congenital anomalies were discovered in 12 per cent of the patients, including imperforate anus (5), duodenal atresia (1), cyanotic heart disease (3), and skeletal deformities of the spine and extremities (2).

The diagnosis of most congenital esophageal lesions is not difficult. The newborn infant usually breathes with difficulty or has excess mucus in the mouth and pharynx. Difficulty is encountered at the first attempt at nursing, with symptoms of choking. In such cases a soft radiopaque rubber catheter should be passed into the esophagus. If an obstruction is encountered, the presence of the lesion can be substantiated by the introduction of a small amount of iodized oil. An obstruction in the esophagus at a level corresponding to the second to fourth thoracic vertebrae is indicative of atresia. Obstruction below this level indicates esophageal stenosis or cardiospasm.

A roentgenogram of the entire infant should be secured, not only to evaluate the chest and mediastinum but to study the gas patterns in the intestinal tract. Gas in the intestines in the presence of an atresia of the esophagus indicates an associated tracheoesophageal fistula. In addition, an associated congenital abnormality of the intestine may be demonstrated.

The surgical and preoperative and postoperative treatment is discussed in detail. On the day following the repair of the esophageal lesion, a gastrostomy is performed and a naso-esophagogastric string is inserted as a routine procedure, except in the case of simple tracheo-esophageal fistulas. Oral feedings are withheld until the integrity of the esophageal anastomosis is established. On the fourth or fifth postoperative day a small amount of Lipiodol is placed in the esophagus under fluoroscopic vision. If there is no evidence of a leak, oral feedings are begun. Between the second and third week postoperatively, gentle retrograde bougienage determines the size of the esophagus. After sufficient time elapses for establish-

ment of an adequate lumen, the endoscopic string is removed and the gastrostomy closed.

Complications included leakage at the suture line of the esophagus and esophageal stricture. Some evidence of stricture developed in two-thirds of the patients. The goal of all esophageal surgery is the absence of stricture formation at the suture line. It is recognized that complications will, at times, result from the precautionary gastrostomy, but these disadvantages are far outweighed by the advantages for the patients in whom dilatations are required.

Six roentgenograms; 4 drawings; 3 tables.

JOHN F. WEIGEN, M.D.
Palo Alto, Calif.

The Association of Cancer of the Stomach and Oesophagus with Herniation at the Oesophageal Hiatus of the Diaphragm. D. W. Smithers. Brit. J. Radiol. **28:** 554–564, October 1955.

The author collected from the literature 96 cases of carcinoma of the stomach or esophagus associated with hiatus hernia and to these adds 12 examples seen at the Royal Cancer Hospital (London) in the past few years. One of the latter group of patients had a tumor of the stomach, and in 11 the tumors were judged to be primary in the esophagus. The stomach tumor was a leiomyosarcoma. Four of the esophageal tumors were of the squamous-cell variety and 5 were adenocarcinomas. The 12 cases histories are presented.

The association of cancer of the esophagus and stomach with sliding hiatal herniation appears to the author to be too common to be due to chance. The predominance of adenocarcinoma of the esophagus over the more usual squamous-cell carcinoma seems to require some explanation. Two factors would seem to be (1) that a small lower portion of the esophagus is lined by glandular epithelium which, at this constricted site, is particularly liable to malignant disease and (2) that there is a preferential spread of carcinoma of the cardia in the submucous lymphatics of the esophagus.

Thirteen roentgenograms; 1 photograph; 2 tables.

J. P. CHAMPION, M.D.
Grand Rapids, Mich.

Hiatus Hernia with Adenocarcinoma Arising in the Region of the Cardia. J. N. Pattinson, G. Osborne, and B. C. Morson. J. Fac. Radiologists **7:** 90–101, October 1955.

The purpose of this paper is to call attention to the occurrence of adenocarcinoma arising in the region of the cardia in association with hiatus hernia, with special reference to the occasional radiological similarity of the malignant stricture, so-called, to the benign stricture of peptic esophagitis. The authors suggest that the coexistence of hernia and carcinoma is more common than has been generally supposed. Nine cases are described. In 4, the lower end of the esophagus was found to be lined with gastric mucosa. In 3 of these there was no invasion of the stomach.

The difficulties of radiologic and endoscopic distinction between benign and malignant stricture of the esophagus in cases of hiatus hernia, and of the detection of carcinoma confined to the supradiaphragmatic loculus of the stomach, are discussed.

Thirteen roentgenograms; 3 drawings; 1 table.

THEODORE E. KEATS, M.D.
University of California, S. F.

The Roentgen Signs of Gastritis. Clinical Analysis. L. Walk. Am. J. Roentgenol. **74:** 567–579, October 1955.

In this paper from Eskilstuna, Sweden, the roentgen signs of gastritis are analyzed, together with the clinical and gastroscopic findings, in a series of 252 cases. Examination in the recumbent and prone positions was performed routinely prior to examination in the erect position. A survey film was taken one to two minutes after a barium swallow, and compression films for relief study were made. Otherwise the procedure was similar to any ordinary gastrointestinal examination.

The roentgen observations included the gastric configuration, the mucosal folds, and intermediary fluid and secretion. In general, the findings were most constant in mucosal atrophy: in 70 per cent of uncomplicated cases these consisted of "dry stomach" and mucosal folds not exceeding 3 to 3.5 mm., in association with histamine achylia. There are, however, cases of histamine achylia without roentgen signs of atrophy.

Catarrhal gastritis with reddening and cobblestone mucosa are not to be diagnosed roentgenologically.

Catarrhal gastritis with swelling is identified by thickened folds of 5 mm. or more. With submucosal swelling there is usually some intermediary fluid, in contrast to gastritis with reddening, where fluid is absent or small in amount.

Eighteen roentgenograms; 10 photographs; 5 tables.

ROBERT H. LEAMING, M.D.
Memorial Center, N. Y.

Acute and Chronic Jejunogastric Intussusception. William S. Caudell and C. Marshall Lee, Jr. New England J. Med. **253:** 635–640, Oct. 13, 1955.

The authors believe that jejunogastric intussusception following gastroenterostomy, with or without partial gastric resection, is more common than is suspected, particularly in its chronic recurrent form. Two cases are reported here.

Clinically, *acute intussusception* of either the afferent or efferent (retrograde peristalsis) loop of jejunum through the stoma into the stomach is marked by moderate to severe epigastric colic followed shortly by persistent vomiting. At the onset, the vomitus may be clear or contain food; as the stoma strangulates the neck of the intussusceptum the vomitus becomes dark or reddish brown. Blood loss may be dramatic and may be mistaken for hemorrhage from peptic ulceration. There is epigastric tenderness with no splinting. A palpable mass has been described in about one-third of the reported cases.

Plain films of the abdomen are usually uninformative, but in the acute case reported by the authors a homogeneous density within the stomach was noted. This was assumed to represent the invaginated, edematous, thickened jejunum. With a barium meal the gastroenterostomy stoma is not usually visualized, the invaginated loop of jejunum causing complete obstruction to the outflow of barium. The barium collects between the valvulae conniventes and outlines the intruding bowel with parallel lines, fan-shaped curves, spirals, or concentric circles. This striated filling defect in the stomach is pathognomonic of the condition.

In the *chronic*, remitting case, the epigastric discomfort is initiated by eating, lasts an hour or more, and ceases spontaneously, with the reduction of the intussusception. Vomiting supervenes only if the obstruction is complete or if the temporary obstruction

lasts long enough. It is only in the presence of active symptoms in these chronic cases that the lesion is demonstrable radiologically. By the use of a small amount of barium, along with manual compression, the feathery outline of the intussusceptum may be outlined. In most of the chronic cases, however, the temporary nature of the pathological physiology precludes objective demonstration even at operation, where it is possible that a small invagination is inadvertently reduced with the anesthesia and/or traction on the peritoneal structures before the surgeon reaches the stomach.

Most patients with this complication have no associated ulcer or polyp and in these the treatment of choice, provided the reduced bowel is viable, is restoration of normal continuity. In the presence of recurrent ulcer the ingenuity of the surgeon, as well as the extent of the previous operation, will determine the type of surgery.

Three roentgenograms; 4 drawings.

SAUL SCHEFF, M.D.
Boston, Mass.

A Contribution to the Radiological Diagnosis of Perforated Gastric or Duodenal Ulcer. Petter Joh. Ström and Aksel Strömme. Brit. J. Radiol. **28:** 579–580, October 1955.

The presence of free gas in the peritoneal cavity is indicative of a perforated ulcer of the stomach or duodenum but is not always demonstrable. Radiological findings have been reported as negative in 10 to 35 per cent of cases. In 2 patients seen by the authors, free air was not seen on the original radiographic study but was visualized after aspiration of the gastric contents. A possible explanation for this is that the fluid contents of the stomach serve as a water-closed valve, blocking the escape of gas into the peritoneum, or it may be that the perforation is closed by debris, which is evacuated by aspiration.

There are no contraindications to aspiration of the stomach contents, and the authors recommend it to reduce the diagnostic error in perforated peptic ulcer.

Five roentgenograms.

J. A. GUNN, M.D.
Grand Rapids, Mich.

Pseudotumors of the Duodenal Bulb. Simon M. Berger. Am. J. Roentgenol. **74:** 580–586, October 1955.

The author presents 5 cases of pseudotumors of the duodenal bulb, with observations on the clinical history, roentgen features, and differential diagnosis. The series includes a pedunculated tumor arising from the gastric cardia, a duodenal diverticulum adherent to the wall of the duodenal bulb, a small acute duodenal ulcer with perifocal edema, a gallstone impacted in the wall of the duodenal bulb, and a probable case of hyperplasia of Brunner's glands. The first 4 of these cases were surgically proved.

Nineteen roentgenograms.

ROBERT H. LEAMING, M.D.
Memorial Center, N. Y.

Fifteen Year Follow-up of an Intestinal Shunt Without Relief of the Primary Obstruction. Thomas H. Williams and Herbert M. Olnick. J. M. A. Georgia **44:** 477–480, October 1955.

When an operative procedure results in the formation of a blind loop of intestine, the basis is laid for the development of a symptom-producing pouch. When entero-enterostomy is performed as a palliative measure in the treatment of intestinal obstruction, the obstructed loop has sometimes been simply by-passed and left in place. Similarly, following resection, side-to-side anastomosis will produce a blind pouch if the closed stump is too long. Intestinal contents may stagnate in such loops, with resultant ballooning and wide pouch formation. Infection, ulceration, and sometimes perforation may develop.

Symptoms include nausea, vomiting, constipation, distention, anemia, diarrhea, fever, and even malnutrition. Episodes suggesting intestinal obstruction are prominent in reported cases. When the pouch is mildly distended, reflex hyperperistalsis may occur, with resulting diarrhea. With more marked distention of the pouch, reflex ileus results. Differential diagnosis must include adhesions and retained surgical sponges in the postoperative patient.

Roentgen findings of positive value help in differentiation. A soft-tissue mass representing the pouch may be seen on plain films. Barium-meal study of the small intestine may show a collection of the medium in the pouch, mixed with intestinal contents. This remains at one location, while the bulk of the barium stream passes on into the colon.

The authors' patient gave a history of four earlier operations for intestinal obstruction, the last of which was a lateral anastomosis to by-pass the obstructed loops, fifteen years earlier.

Four roentgenograms; 1 drawing.

DONALD DEF. BAUER, M.D.
Coos Bay, Ore.

Lymphatic Cyst of Transverse Colon. Report of a Case Radiographically Simulating a Neoplastic Polyp. R. R. Koenig, D. B. Claudon, and R. W. Byrne. Arch. Path. **60:** 431–434, October 1955.

A case of benign pedunculated cystic lymphangioma in the submucosa of the transverse colon of a 54-year-old man is reported. During a routine annual physical examination, barium-enema studies, including pre-evacuation and post-evacuation films and double-contrast air films, disclosed a filling defect, thought to be caused by a polyp. The lesion was to the right of the mid-line in the transverse colon and measured 2 to 3 cm. in diameter. The appearance suggested the possible presence of a narrow stalk, 3 to 4 cm. long, the base of which was proximal to the main mass. Palpation of the transverse colon at operation revealed a resilient, non-compressible pedunculated mass within the lumen, midway between the hepatic and splenic flexures. When the mass was isolated between the surgeon's fingers, the anterior wall of the colon bulged in a thinned area 1.2 × 1.5 cm. between tineae and it became apparent that the lesion was not a solid mucosal polyp, but a thin-walled cyst. A segment of the colon 6 cm. long was resected. Incision of the mucosa exposed a unilocular, thin-walled, submucosal cyst filled with clear amber fluid. Lax mucosa and underlying tissues formed a short stalk or pedicle.

Two roentgenograms; 3 photographs; 2 photomicrographs.

A Diagnostic Survey for Extragastrointestinal Lesions of the Left Upper Quadrant. Jack Greenfield. South. M. J. **48:** 1056–1061, October 1955.

Because of the contiguity of the organs and tissues

to each other in the left upper quadrant of the abdomen, lesions arising from them, particularly those which are outside the gastrointestinal tract, present difficulties in diagnosis. It is suggested that a diagnosis can be made in the majority of these cases by the employment of a complete diagnostic survey, consisting of roentgenograms of the chest and abdomen, followed, in order, by fluoroscopy, a gastrointestinal series, barium enema study, pyeloureterograms, and such laboratory and special tests as may be indicated.

For ease of consideration in such a plan, the commoner left upper quadrant extragastrointestinal lesions are tabulated in groups according to their anatomic location as retrogastric, anterogastric, infragastric, left paragastric, hepatic or subhepatic, and phrenic or subphrenic.

Six illustrative cases are reported.

Two roentgenograms; 1 photograph; 2 tables.

Morphological Study of Abdominal Gas Shadows. Samuel L. Beranbaum and Kakarla Subbarao. Am. J. Digest. Dis. **22**: 281–287, October 1955.

Twelve cases are very briefly presented and illustrated, with almost no discussion, showing a variety of lesions in and out of the gastrointestinal tract which may be recognized or suspected by careful observation of gas shadows within the abdomen. These include neoplasms of the stomach and colon, inflammation of the colon and gallbladder, abscesses, hernia, and fistulas.

Twenty-one roentgenograms.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Annular Pancreas. A. J. Aballí, Z. Prendes, and L. de Armas. Rev. pediat. cubana **27**: 613–620, October 1955. (In Spanish)

The authors present a case of annular pancreas with mongolism. The procedure of choice in such a case is a duodenojejunostomy, and in this instance the infant was operated upon successfully according to that method. If the duodenal obstruction by the annular pancreas is accompanied by other serious malformations, the prognosis is serious; but if it is the only lesion present, the patient can be cured in the majority of cases by the establishment of a duodenojejunostomy. The present case resulted somewhat curiously because of an initial deficient functioning of the new opening. That this often occurs has been pointed out frequently. During the early days certain authors proposed the oral introduction of a sound to be carried through the duodenojejunostomy opening. JAMES T. CASE, M.D.
Santa Barbara, Calif.

Roentgen Examination in Cases of Occlusion of the Mesenteric Vessels. Ingemar Hessén. Acta radiol. **44**: 293–305, October 1955.

The author reports 20 cases of occlusion of mesenteric vessels as a result of either thrombosis or an embolus. In all except 2 cases, the occlusion originated in either the superior mesenteric artery or the superior mesenteric vein.

An analysis of the roentgen findings in this series serves to demonstrate the difficulty in making the diagnosis from film studies. In 5 cases they are described as negative, in 5 as uncharacteristic, and in 9 as positive. The only change which may be considered typical of vascular mesenteric occlusion is local paresis of a segment of small bowel. This can be demonstrated in some cases by administration of barium orally, though the condition of the patient rarely permits an examination of this type.

Changes demonstrable on plain films consist of intestinal dilatation, either proximal to or including the infarcted area, and gas and fluid filling of the intestine. The interval between onset of symptoms and the first roentgen examination varied from one hour to eight days, the longer periods being noted more frequently in the cases of venous thrombosis as opposed to those of embolism or arterial thrombosis. No direct relationship between duration of clinical signs and extent of the roentgen signs was observed.

Eleven roentgenograms. DAMON D. BLAKE, M.D.
Bowman Gray School of Medicine

Gallstone Ileus. A Report of 12 Cases. Stephen L. Deckoff. Ann. Surg. **142**: 52–65, July 1955.

The author reports a series of 12 cases of gallstone ileus seen at the Queens General Hospital, N. Y., in an eleven-year period. This group represents 1.3 per cent of 924 cases of intestinal obstruction diagnosed during this time. A definite preoperative diagnosis was obtained or strongly suspected in 6 of the 12 cases. The roentgen examination was considered diagnostic in 3.

In recent years, the most valuable aid in the diagnosis of gallstone ileus has been afforded by the roentgenologist. Flat, upright, and lateral films of the abdomen should be made; in addition, spot-films of the liver region should be taken in several positions. Intestinal obstruction, with dilated loops of bowel, is seen consistently. While this is not in itself diagnostic of gallstone ileus, the site of obstruction may be suggested and occasionally the obstructing stone may be seen. Usually, however, the stones are composed chiefly of cholesterol and are not radiopaque. Outlining of the biliary tree by air or contrast medium is presumptive evidence of a fistula connecting the biliary and gastrointestinal tracts, and is of great diagnostic significance, but unfortunately this finding is often recognized only in retrospect. Barium sulfate given by mouth or through an indwelling intestinal tube may outline the obstructing stone, but is regarded as a dangerous practice, rarely necessary and to be avoided if possible. A barium enema is less hazardous and may outline a stone obstructing the colon or demonstrate a cholecystocolic fistula. Finally, gallstone ileus may be suspected if a stone previously seen in the gallbladder area is no longer visualized. The differential diagnosis must take into consideration all causes of intestinal obstruction.

The treatment of choice is enterostomy, with removal of the stone as soon as possible. In addition to obesity, advanced age, and associated disease, the long period of delay between onset of symptoms and treatment is a major cause of high mortality in patients with gallstone ileus. In the present series, there was 1 death, which represents a mortality rate of 8.3 per cent. It is believed that this low figure is a reflection of improvement in preoperative and postoperative care.

Four roentgenograms.

Studies Concerning the Use of the New Biliary Contrast Media in Health and Disease. F. Leupold and F. Heuck. Fortschr. a. d. Geb. d. Röntgenstrahlen **83**: 464–470, October 1955. (In German)

According to several investigators the use of Biligrafin

(Cholografin) is contraindicated when liver damage is present. It was reported that in 8 out of 23 patients with liver disease in whom the bile ducts could not be visualized, a marked shift of serum protein fractions was found, with increase of alpha and beta globulin.

In a group of 15 normal subjects the authors made the following tests before and three to six days after Cholografin injection: (1) Takata Ara, (2) thymol, (3) bilirubin, (4) alkaline phosphatase, and (5) serum cholesterol. In this series the tests failed to disclose any liver damage. Similar tests were made in a second series of 31 patients with symptoms and signs of liver damage. In only 1 case did a previously negative Takata reaction become positive, while in 2 cases this reaction changed from positive to negative following Cholografin injection. Changes of bilirubin and phosphatase in cholangitic liver cirrhosis were no more pronounced following the injection than could be expected normally in the course of the disease.

The injection was well tolerated in a group of 320 cases. In only 1 case without liver disease did collapse occur two minutes following the injection. The blood pressure became so low that it could no longer be recorded. In spite of aggressive therapy, improvement occurred only after four to five hours. There was no allergy, and liver tests were normal before and after the injection.

Optimal filling of the bile ducts was seen thirty minutes after Cholografin injection in cases with and without previous cholecystectomy. A visualization which was delayed beyond forty minutes was considered normal in overweight patients who had received too small a dose, but was otherwise held to be suggestive of liver damage. An overdose of Cholografin resulted in prompt renal excretion in spite of normal liver function. A moderate degree of liver opacification was frequently observed, but was absent when the drug was excreted rapidly. Non-visualization of the gallbladder and bile ducts did not rule out hepatic excretion altogether but suggested the possibility of a low concentration of the contrast material. In such instances the opaque material could sometimes be detected only in the duodenum or jejunum.

Abnormal serum protein fractions did not interfere with the liver excretion, and normal excretion occurred repeatedly in spite of liver damage as indicated by symptoms, the Takata reaction, and the thymol test. There was no definite connection between abnormal bilirubin values and liver function. A delayed or absent liver excretion, however, was noted in cases with increased phosphatase and in cholesterinemia.

When the liver function is too poor, the drug will be excreted instead by normally functioning kidneys. Cholografin is contraindicated only when various tests reveal poor kidney function in association with liver damage.

One roentgenogram; 1 table.

ERNEST KRAFT, M.D.
Newington, Conn.

Experiences with Intravenous Cholangiocystography with Biligrafin. U. Feine. Fortschr. a. d. Geb. d. Röntgenstrahlen **83:** 445–464, October 1955. (In German)

The author's experience with Biligrafin (Cholografin) is based on 405 cases including 53 postcholecystectomy cases. The following indications for intravenous cholangiocystography have been formulated: (1) non-visualization or equivocal findings with the oral method; (2) strong suspicion of pathologic changes of the biliary system; (3) faulty absorption of the orally administered medium by the gastrointestinal tract; (4) desirability of demonstrating the bile ducts.

The intravenous method has never proved harmful, and there are no definite contraindications to its use, but it has been considered with hesitancy in acute cholangitis, congestive failure, chronic jaundice, and severe liver damage. Visualization of the biliary system has been possible in 90 per cent of the cases.

For the diagnosis of gallbladder disease the intravenous method has the following advantages over the oral method: (1) The gallbladder can be more frequently visualized even when the pathologic changes are far advanced. (2) When the gallbladder cannot be visualized but the medium is excreted by the liver, a diagnosis of advanced cholecystitis and lithiasis can be established. (3) Diagnosis of chronic cholecystitis is probable when the oral method reveals only faint visualization while the intravenous method discloses good filling. (4) Diagnosis of cholecystoptosis with poor fixation of the gallbladder in the liver bed can be established.

For the diagnosis of bile duct changes the following standards of measurement have been established: The hepatic duct has an average width of 3.9 mm., while the common bile duct is normally 4 to 6 mm. wide. A duct measuring more than 7 mm. in width is considered to be dilated. Visualization of the smaller branches of the hepatic duct always suggests a stenosis further down toward the common duct. In total occlusion of the common duct, with stagnation of bile, there is non-visualization of the biliary system. In such instances the drug is excreted by the kidneys instead of the liver. Physiologic renal excretion of an overflow of the drug, however, occurs frequently in the beginning, even in normal cases.

In the author's postcholecystectomy group the bile ducts could be visualized in 91 per cent, with evidence of dilatation in 60 per cent. In the total series of 405 cases there were 40 with non-visualization or faint visualization, including 13 with severe liver damage and 21 with marked icterus.

The intravenous administration of Cholografin has proved to be a safe and dependable liver function test. Non-visualization denotes either liver damage or obstructive jaundice.

Cholangiocystography is useless in chronic icterus with serum bilirubin values over 6 mg. per cent, and when feces are acholic, liver excretion is practically absent. Visualization is also improbable in hepatic and cholangitic cirrhosis and in marked liver enlargement due to metastatic tumors.

The author concludes that the Cholografin method is far superior to other examinations. Bile ducts can now be visualized in 98 per cent of cases with normal liver excretion, and dilatation of bile ducts can be detected in 50 per cent of all pathologic cases.

Sixteen roentgenograms; 5 tables.

ERNEST KRAFT, M.D.
Newington, Conn.

A New Method of Study of the Biliary System: Blocked Cholangiocholecystography. A. Lura and A. Vivarelli. Radiol. med. (Milan) **41:** 945–958, October 1955. (In Italian)

The difficulties of demonstrating the details of the

biliary tree by intravenous cholangiography can be compared to the problems in intravenous urography. Since, in the latter procedure, compression exerted over the area of the ureters enhances detail, similar attempts have been made in Biligrafin studies.

The authors obtain compression on the ampulla of Vater and better demonstration of the biliary tree by the introduction of a tube carrying on its tip a small inflatable balloon of soft rubber. Under fluoroscopic control the balloon is advanced into the second portion of the duodenum and then distended with 80 c.c. of air. The safety of this procedure was tested experimentally and it was found that the balloon will rupture long before the duodenum is injured. After the balloon is distended, the tube is fixed to prevent its further advance. Forty cubic centimeters of Biligrafin are injected. Approximately forty minutes after the injection, in some cases, simultaneous visualization of the hepatic and common ducts, gallbladder, and intrahepatic biliary ducts of the third order was obtained. While without the blocking provided by the intraduodenal balloon the gallbladder did not become visible for one or two hours, with the method described visualization was obtained after ten to twenty minutes. Several illustrative cases are presented.

Thirty-four figures, including 27 roentgenograms.

ALEXANDER R. MARGULIS, M.D.
University of Minnesota

Intravenous Cholecystography with a New Medium: Experience with Sodium Acetrizoate (Urokon Sodium) Seventy Per Cent. Theodore L. Orloff. Arch. Surg. **71:** 620–622, October 1955.

Sodium acetrizoate (Urokon Sodium) 70 per cent, used primarily in intravenous urography, nephrography, translumbar aortography, and angiocardiography, can also be employed for intravenous cholecystography. The opacity of the cholecystograms is inversely proportional to renal function, the concentration in the gallbladder being best in patients with diminished renal function. In cases with normal renal function, opacification of the gallbladder, although sufficient for visualization, is not considered as completely diagnostic as with the oral technic, since the proper density is lacking.

Four roentgenograms.

JOHN F. WEIGEN, M.D.
Palo Alto, Calif.

Personal Experience with Postcholecystectomy Oral Cholangiography. Eilif C. Hanssen and Paul H. Deeb. West. J. Surg. **63:** 619–622, October 1955.

Using Telepaque, the authors of this paper were able to visualize the common bile duct in 12 out of 14 postcholecystectomy patients. Six tablets were given orally, with one-half glass of water, thirteen hours and again five hours prior to roentgenography. Each dose was followed, after thirty minutes, by a teaspoonful of paregoric. If the bile ducts were seen on the first set of films, amyl nitrite inhalations were given and further films were obtained at half-hour intervals. If the bile ducts failed to empty, a fatty meal was given before further studies were made.

Visualization was regarded as good in 2 cases (16 per cent), fair in 5 (42 per cent), and faint in 5 (42 per cent). The only abnormality demonstrated in this series was common duct dilatation. This was reported whenever the common duct diameter exceeded 6 mm. Transient diarrhea was the only reaction observed.

Brief reports of each case are included, but in only 1 is the response to amyl nitrite and the fatty meal mentioned. In that instance, partial emptying of the common duct was demonstrated.

Seven roentgenograms.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Operative Cholangiography. J. H. Gifford and S. C. Kahlstrom. West. J. Surg. **63:** 605–606, September 1955.

This study was made in the interest of evaluating the procedure of operative cholangiography. Two groups were studied, each consisting of 100 patients undergoing cholecystectomy for cholelithiasis. In the first group, the decision to explore the common bile duct was based solely upon clinical indications and palpation. Among 29 of these cases in which exploration of the common duct was undertaken, stones were found in 9. In the second group, operative cholangiography was performed and in 23 cases the decision to explore the duct was based on the results of that study. Stones were found in 21 of these.

Residual stones were subsequently discovered by postoperative cholangiography or exploration in 6 of the first group and were strongly suspected on clinical grounds in 8 others. In only 3 of the second group were stones left behind.

It is concluded that operative cholangiography is much to be preferred to clinical indications as a guide for common duct exploration.

One table.

Cholangiography in Surgery of the Biliary Tract, at the State University of Iowa. John A. Gius and C. J. Johnson. J. Iowa M. Soc. **45:** 513–518, October 1955.

The authors believe that operative cholangiography should be a routine procedure in surgery of the biliary tract for benign disease. They report results and recommendations based on a series of 274 patients in whom 282 operations were performed for non-malignant biliary tract conditions.

In 163 of these operations (57.8 per cent), immediate cholangiography was performed and in 61 instances (21.6 per cent) the common duct was explored; the x-ray films were unsatisfactory in 5 cases (3.1 per cent); the pancreatic duct was visualized on the cholangiogram in 25 cases (15.3 per cent).

Cholecystectomy with cholangiography was carried out in 126 cases. Roentgen findings in 10 (8 per cent) of these were regarded as indications for exploration of the common duct; stones were found in 5 of these cases at surgery, no abnormalities being encountered in the remainder. The films of 13 other patients (10.3 per cent) studied after operation revealed changes that were suggestive but not diagnostic of residual common duct disease.

Sixty-three (38.6 per cent) of the cholangiograms were technically imperfect, although adequate for interpretation. Common causes of defects and their frequency in the present series are listed.

Sixty-one operations were performed on the common duct. One or more indications for exploration (including cholangiography) were present in 51 instances; in 10 additional patients, exploration was performed on the basis of x-ray findings only. In half of the latter group, common duct stones were found. Of 47 cholangiographic studies carried out in conjunction with

common duct exploration, 22 demonstrated disease in the duct.

The results of operative cholangiography should always be correlated with the findings on operation; the method is not advocated as a substitute for other methods of evaluation, but is to be used in conjunction with them. The importance of repeated cholangiograms in doubtful cases is stressed. It is also urged that cholangiography be performed *after* common duct exploration, as a check against incomplete removal of stones.

Six roentgenograms; 2 photographs; 4 tables.

THE MUSCULOSKELETAL SYSTEM

The Roentgenologic Aspects of Chordoma. John R. Utne and David G. Pugh. Am. J. Roentgenol. **74:** 593–608, October 1955.

The chordoma is a rare malignant tumor derived from remnants of the notochord and locally invasive, recurring following attempts at surgical removal, but seldom metastasizing. A review of the literature is presented encompassing particularly the embryology of the notochord and citing the cases previously reported in the literature, which, with the present series total 505.

This article is based upon 72 cases from the files of the Mayo Clinic from 1910 through 1953, with original roentgenograms available for 41 cases. All but 13 of these cases have been reported previously. The chordomas in these 72 cases were distributed as follows: cranial, 25 per cent; vertebral, 19 per cent (chiefly in the cervical region); sacrococcygeal, 56 per cent. The tumor does not ordinarily arise from notochordal tissue in its normal location in the nucleus pulposus of the intervertebral disk but only from those cells which are ectopically placed. It is probable that trauma may be a predisposing factor in at least 40 per cent of the cases; and there is a significant male preponderance. The age incidence ranges between eight and seventy-six years with a mean of 46.8 years.

The gross pathology of the tumor is reviewed, as is the microscopic pathology, with a wide variation of appearances and size being noted. Metastasis was proved in only 1 instance, to the scapula.

The presenting complaints and physical findings varied according to the location and direction of spread of the tumor.

The roentgenographic findings, regardless of location, were as follows: Some degree of bony change was evident in 83 per cent of the cases. A soft-tissue mass was present in 80 per cent. There were no distinguishing features about the bone destruction, but the typical location in which it occurred was indicative of a mid-line tumor at the base of the skull in the case of cranial lesions, or destruction of some portion of the vertebra in the vertebral lesions. In the latter instance the osteolytic process began in the vertebral body and in half of the cases extended to involve three or more adjacent vertebrae. Pathologic fracture with collapse was found only in the lower thoracic and lumbar regions, where weight-bearing was more excessive than in the cervical and upper thoracic regions. New bone formation was rare except as a complication of compression injury or fracture with a stimulation of osteoblastic activity thereby.

A visualization of the soft-tissue mass comprising the tumor occasionally can be accomplished, particularly in the case of the nasopharyngeal lesion, and with the aid of ventriculography in the intracranial lesions. In the cervical spine direct evidence of the soft-tissue tumor outline was present in each of the 6 cases in the series. In the sacrococcygeal region there was positive evidence of bone destruction in most cases as well as a soft-tissue mass. The mass is predominantly antesacral in most of the cases, tending to invade predominantly in the anteroposterior plane. Occasionally an amorphous mass of calcification within a necrotic and degenerating tumor was the most frequent finding (approximately 50 per cent of sacrococcygeal group).

In the overall group roentgenographic examination of a chordoma reveals evidence of bone involvement or a soft-tissue mass in more than 90 per cent of the cases. The resemblance of the clinical and roentgenographic manifestations of cranial and vertebral chordomas to those of other tumors of the brain and spinal column preclude differentiation in most cases, but a correct preoperative diagnosis is possible in nearly half of the sacrococcygeal cases.

Thirteen roentgenograms; 3 photomicrographs; 6 tables.

I. MESCHAN, M.D.
Bowman Gray School of Medicine

Fibrosarcoma Arising in an Apparently Benign Fibrous Lesion of Bone. Allan Hall, S. R. Bersack, and R. E. Vitolo. J. Bone & Joint Surg. **37-A:** 1019–1027, October 1955.

A slowly growing osteolytic lesion of the upper tibia, diagnosed by curettage, on repeated occasions, as fibrous dysplasia or benign central fibroma and finally requiring mid-thigh amputation, is reported. The amputation specimen showed frank areas of fibrosarcoma. Roentgenograms, taken over a period of approximately six years, demonstrated an osteolytic lesion, at first confined by the cortex although widening the shaft and causing marked cortical narrowing. The films taken just prior to amputation showed the tumor definitely breaking through the cortex.

The authors believe that this represents an example of a benign lesion undergoing malignant change. Their assumption is that the original lesion existed in a benign phase for a considerable time prior to its detection, since a fully established expansile rarefaction, measuring 7 cm. in length, was observed only three weeks after the first complaint. The malignant transformation they date from the first appearance of symptoms, in spite of the absence of histologic evidence. In such cases reliance is to be placed upon the clinical and radiological observations.

The therapeutic aspects of the case are of interest. Though the patient was referred for irradiation, this was felt to be unjustifiable, and amputation was recommended. In advising against roentgen therapy for osteolytic fibrous lesions of bone, the authors argue that, if sarcomatous changes are already present, radiotherapy will not result in a cure and, should sarcoma later become apparent, the irradiation might (unjustifiably) be blamed. Complete surgical extirpation affords the best chance of cure.

Ten roentgenograms; 5 photomicrographs.

RICHARD G. LESTER, M.D.
University of Minnesota

Osteosclerosis in Renal Failure. R. W. Brookfield, E. L. Rubin, and M. K. Alexander. J. Fac. Radiologists **7:** 102–108, October 1955.

Although the renal pathology of chronic glomerulo-

tubular insufficiency is varied, the bony changes, when they appear, are a mixture of rickets and osteitis fibrosa, the proportions varying with age. It has been shown that, as a rule, the earlier the onset of renal failure, the more closely the histologic appearances resemble rickets; when the condition develops toward the end of the growth period, osteitis fibrosa tends to predominate. The finding in renal failure of yet another type of osteodystrophy, namely osteosclerosis, has been reported sporadically. Two such cases are presented here. In one there was a mixed picture of sclerosis and decalcification. The second case showed osteosclerosis and questionable areas of relative increased translucency of some of the bones.

The authors have no adequate explanation why, in some cases decalcification should be replaced by, or exist alongside, excessive new bone formation. It is suggested that if, in renal failure, a hypertrophic response is evoked in the parathyroids, osteosclerosis having already been established, the mixed picture of sclerosis and decalcification might be produced.

Ten roentgenograms; 5 photomicrographs; 1 table.

THEODORE E. KEATS, M.D.
University of California, S. F.

Massive Osteolysis (Acute Spontaneous Absorption of Bone, Phantom Bone, Disappearing Bone): Its Relation to Hemangiomatosis. L. Whittington Gorham and Arthur Purdy Stout. J. Bone & Joint Surg. **37-A:** 985–1004, October 1955.

A syndrome characterized by complete absorption of a bone, a portion of a bone, or several bones is described. Twenty-four cases from the literature are reviewed. Thirteen of the patients were twenty-one years of age or less. Slowly progressive absorption over several years occurs. The process usually stabilizes after an indefinite period, but notable regrowth of bone has not been seen. Two patients have died as a result of the disease process (and an additional 9 could not be traced).

The authors were able to obtain for review microscopic sections from 8 of the reported cases. The histologic picture, like the clinical and roentgen findings, was remarkably consistent in all the cases examined. In each instance there was an ingrowth of blood vessels, usually thin-walled capillaries, which were dilated and filled with red blood cells. To this process the authors apply the term "hemangiomatosis." The mechanism by which the bony trabeculae are demineralized and absorbed was not apparent from a study of the sections, since no osteoclasts were recognized.

Six roentgenograms; 13 photomicrographs; 1 photograph; 1 drawing; 1 table.

RICHARD G. LESTER, M.D.
University of Minnesota

Infantile Cortical Hyperostosis. Presentation of a Case Treated with Hydrocortisone and Corticotropin. Review of the Literature. Alberto de Córdova and Elena Sánchez Pessino. Rev. pediat. cubana **27:** 597–612, October 1955. (In Spanish)

The authors review the history, incidence, and etiology of infantile cortical hyperostosis, and then give the history of a white female child, born in the United States. The diagnosis may be suspected clinically but its elaboration depends upon the demonstration of the characteristic hyperostotic lesions. Consideration of the differential diagnosis is almost superfluous, since the signs of hyperostosis, first described by Caffey, are definite, and confusion with any other lesion is hardly possible. Nevertheless, it is important to eliminate syphilis. The differentiation from scurvy is based on the absence of epiphyseal lesions and the appearance of the distal cortex, which is always involved in scurvy. Absence of subperiosteal hemorrhages and the presence of maxillary lesions speak for hyperostosis.

The prognosis, though favorable, is not as good as estimated by Berrey (Pediatrics **6:** 78, 1950. Abst. in Radiology **56:** 779, 1951). Antibiotics, antihistamines, and vitamins have been utilized without visible results. Recently cortisone and corticotropine have been reported to produce some dramatic effects, but the authors' experience with these preparations has not been so favorable. His patient was seen four months after the end of treatment with cortisone and five months after the beginning of the disease. The radiographic examination showed marked regression of the hyperostosis of the lower jaw.

JAMES T. CASE, M.D.
Santa Barbara, Calif.

A Case of Fluorosis. T. Fichardt, J. L. Van Rhyn, and G. W. Van Selm. J. Fac. Radiologists **7:** 130–135, October 1955.

Skeletal osteopetrosis is described in a patient who had for twenty years obtained his drinking water from a well containing excessive fluorides. Radiologically the bones generally showed complete loss of fine architectural detail and were of a sclerotic granular density. The margins of the vertebral bodies and long bones lacked smoothness and appeared fluffy. There was osteophytic bridging of vertebral interspaces, causing rigidity, especially in the cervical and dorsal regions. The lumbar transverse processes appeared to be draped in cobwebs composed of bony spicules and calcifications within ligamentous attachments. Hip and shoulder joints showed lipping on the articular edges. The inferior margins of the pubic bones showed bony spiculation. The costal interspaces were so covered by bony overgrowth on the rib edges that heart and lung detail were obscured. Mottling of tooth enamel was present.

The authors include a brief review of the literature and a summary of the pathological findings in fluorosis.

Eight roentgenograms; 1 photograph.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

The Lumbar Intervertebral Disc Disease Syndrome. Clinical Correlation of One Hundred and Seventy-Five Cases. W. Eugene Stern. West. J. Surg. **63:** 647–653, October 1955.

In a series of 175 patients suffering from the clinical syndrome of lumbar intervertebral disk disease, the preoperative observations are reviewed in the light of the surgical findings. Practically every patient gave a diagnostic clinical picture for disk protrusion, with back pain, limited lumbar mobility, limited straight leg raising, etc. The presence or absence of nerve root compression was less clear cut.

Conventional roentgenograms showed abnormalities in alignment or in shape of the vertebral bodies in 96 patients. There was intervertebral disk space narrowing in 108 cases, which in 64 was limited to one inter-

space. In 16 of cases, the disk herniation was not found at the level of narrowing, but at an adjacent interspace. In 61 cases there was sclerosis of the adjacent vertebral bodies or hypertrophic spurring about the attachments of the annulus fibrosus to the vertebral rim.

Myelography was performed in all but 1 case. In 32 patients there was discrepancy between operative findings and myelographic interpretation. In 7 cases a defect was seen myelographically where none was found at surgery. In 24 cases disease was found surgically where no defect was apparent in the myelograms.

It appears that, since false negative myelograms are considerably more common than false positives, the presence of a myelographic defect is probably more dependable than a negative study.

Four tables. DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Calcification of the Intervertebral Discs in a Child. Report of a Case Following Poliomyelitis. Alexander D. Crosett, Jr. J. Pediat. **47:** 481–484, October 1955.

Calcification of the intervertebral disks in childhood is said to be infrequent. Silverman (Radiology **62:** 801, 1954) collected 8 cases from the literature and added 7 of his own, in only 2 of which were there suggestive clinical findings. The author reports the case of a 29-month-old white female with roentgenologically demonstrable disk calcification discovered after an attack of paralytic poliomyelitis. Calcification was not present in the child's monozygotic twin.

The suggestion is made that calcification of the intervertebral disks in childhood is a separate entity related to a definite type of disease process involving the spine and perhaps the spinal cord.

Two roentgenograms.

Tumors of the Ribs. Lew A. Hochberg and Philip Crastnopol. Dis. of Chest **28:** 406–415, October 1955.

Primary rib tumors are more often benign than is evident from the literature on the subject; indeed, as frequently benign as they are malignant. It is difficult, however, to establish benignancy or malignancy radiologically, at surgery, or even microscopically. For these and other reasons, all primary tumors of the rib should be removed unless contraindications to surgery exist. Of 212 collected cases of primary rib tumor, 111 were benign and 101 were malignant. The largest category in the benign group is fibrous dysplasia, followed by chondroma and osteochondroma. The largest category in the malignant group is chondrosarcoma followed by endothelioma (Ewing's tumor) and fibrosarcoma.

Several illustrative cases are reported.

Ten roentgenograms; 8 photographs; 1 table.
DONALD DEF. BAUER, M.D.
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GYNECOLOGY AND OBSTETRICS

Recent Advances in Hysterosalpingography and Angiography in Gynaecological Diagnosis. Olof Norman. J. Obst. & Gynaec. Brit. Emp. **62:** 816–819, October 1955.

This is a general discussion of aspects of hysterosalpingography and angiography of current interest. The ideal contrast medium for hysterosalpingography has not yet been found. More and more examiners now prefer to use water-soluble contrast media made viscous by the addition of thickening agents. The disadvantage of such material is the occurrence of granulomas secondary to the presence of the thickening agent. For the last three years, the author has tried a new contrast medium. Perjodal H, a di-iodized pyridon of ordinary type with the addition of dextran as a thickener.

In 160 experiments carried out on rabbits, this medium produced no demonstrable reaction in the tissues. A clinical trial of the medium for hysterosalpingography was made on more than 600 patients. The patients reported only slight discomfort, and local anesthesia was not found necessary. Granulomas were present in 3 out of 84 operative specimens, as compared with their occurrence in 16 of 18 cases in which carboxymethylcellulose was used.

One of the reasons for the increasing use of water-soluble contrast media instead of the iodized oils is the risk of a reflux from the uterine cavity into the blood stream. This reflux occurs in about 5 per cent of all examinations. Its radiological appearance is both characteristic and readily recognized. The contrast medium spreads into the fine vessels of the uterus. If it persists for any length of time in small tortuous vessels only, the reflux is probably confined to the lymphatics; uterovenous reflux is characterized by entrance of the contrast medium into the larger veins. It appears that a condition necessary for this occurrence is a lesion in the mucosa. The mechanical injury incident to diagnostic curettage may be sufficient. The author, therefore, always waits a few days before doing hysterosalpingography following curettement.

The x-ray appearance of contrast medium injected into the parametrium is extremely characteristic. The material follows the outline of the broad ligament and of the base of the pelvis.

There is another type of perforation which produces a typical x-ray appearance. This is usually seen as an irregular cylindrical channel extending into or passing through the myometrium. It is usually associated with venous reflux. Perforations of this type are frequently seen at the periphery of a myoma, and there is filling of the myomal vessels, which are characteristically fairly straight.

The author has found hysterography valuable in the diagnosis of cancer of the corpus, especially in cases of suspected cancer in which curettage fails to show evidence of disease. The anatomical information obtained is not only of value in the establishment of a primary diagnosis but is also a great help to the therapist in forming a clear impression of the uterine cavity when radium packing is the treatment of choice.

Pelvic arteriography represents the latest advance in gynecological radiology. The method is a new approach to differential diagnosis between salpingitis, tubal pregnancy, and ovarian tumors. While experience with this procedure is still limited, there is reason to hope that, with time, it will open up new diagnostic possibilities in obstetrical and gynecological radiology.

This paper, presented at the Fourteenth British Congress of Obstetrics and Gynecology, is followed by fairly lengthy discussions by Rubin (of New York), Williams (of Guildford), and others. Rubin has found Salpix, a recent water-soluble product combining acetrizoate with polyvinylpyrrolidol, to offer advantages over previous combinations of organic iodine with various substances to increase viscosity. He points out

the difference in the requirements for hysterography and hysterosalpingography. In salpingography radiopacity is extremely important. Viscosity also needs to be greater, since, if there are points of narrowing with some degree of permeability, a less viscous medium can pass through without demonstrating the site of partial obstruction. In hysterography, on the other hand, a too intensely radiopaque substance may overshadow a uterine tumor. The degree of viscosity is also less important than in salpingography.

The tendency, Rubin believes, has been to use excessive amounts of contrast material for both hysterography and hysterosalpingography. In general, it has been found that in the majority of cases 4 to 5 ml. are necessary for the latter procedure, although smaller amounts may frequently suffice. For hysterography 1.5 to 2 ml. is practically always adequate.

Williams uses a water-soluble medium injected under fluoroscopic control. He discusses particularly the effect of posture and the state of the bladder on the results of examination. His remarks are illustrated by 10 roentgenograms.

THEODORE E. KEATS, M.D.
University of California, S. F.

The Clinical Value of Hysterosalpingography. Ellis Barnett. J. Fac. Radiologists **7**: 115–129, October 1955; 184–196, January 1956.

This report is based on a study of 535 patients who were subjected to hysterosalpingography, predominantly for investigation of sterility problems.

The examination is done without anesthesia, under fluoroscopic guidance. The author uses Lipiodol in cases where the main object of the examination is exclusion of uterine disease. From 4 to 6 c.c. of this medium are usually adequate. When tubal disease or the presence of a pelvic mass is suspected, Viskiosol "6," a water-soluble preparation, is the medium of choice. Approximately 10 to 12 c.c. are required in the average case.

In Part I of the paper, multiple developmental anomalies of the uterus, spastic uterus, and uterine tumors are considered. The uterine anomalies comprise those of shape (double uterus, unicornuate uterus, arcuate uterus, etc.), size, and position. Spastic uterus (or "ghost uterus") is a name reserved for the condition in which the uterus is contracting actively and powerfully and any medium injected into the cavity is forcefully expelled in spite of attempts to maintain filling. The appearance of uterine fibromyoma in various locations is described and 2 cases of probable adenomyosis are briefly reported. Both showed an enlarged uterine cavity with multiple saccular protrusions. No malignant neoplasms were encountered.

Tubal conditions are considered in Part II of the paper.

In tuberculous salpingitis, the x-ray appearances are not pathognomonic. However, the presence of this condition can sometimes be inferred from the combination of a suitable history with such tubal changes as irregularity, multiple strictures, calcified debris, or fistulas. All these findings favor the diagnosis of tuberculosis, as does the occurrence of straight, pipestem tubes. Only the minority of cases of pelvic tuberculosis will show changes of specific diagnostic value. The majority will show tubal occlusion or hydrosalpinx, with or without an abnormal mucosal pattern. The x-ray appearances for tuberculous endometritis are not specific but, since the endometrium is so accessible to curettage, the diagnosis is almost invariably made by this latter method.

In the demonstration of hydrosalpinx, hysterosalpingography has proved to be of the utmost value. Experience in this series has shown that, although Lipiodol will enter the dilated tube in a large number of cases, the diagnosis is sometimes left in doubt. A water-soluble medium will enter and completely outline the tubes in the majority of these cases, the diagnosis being further established by failure of the medium to be absorbed within half an hour. The water-soluble medium is therefore the one of choice. It is emphasized that hydrosalpinx is not necessarily synonymous with a complete tubal occlusion. In addition, the possibility of a false positive CO_2 test in this condition must be borne in mind, although its occurrence is rare. It is probable that this false positive result is due to the gas passing through the dilated tubal sac.

The author considers that pelvigraphy can be used as a routine procedure when a pelvic mass is suspected, without necessitating prolonged examination. He uses 25 c.c. of Viskiosol, either undiluted or with the addition of 15 to 25 c.c. of 0.5 per cent procaine. In the present series injection of the contrast material in this quantity did not induce a higher incidence of after-pain than was observed in other patients. Severe pain is more likely to be induced if the medium is injected rapidly, thus producing a rapid extensive peritoneal spill.

The results of the CO_2 test and hysterosalpingography were correlated in the assessment of tubal patency in 378 cases. The hysterosalpingogram was found to give a more reliable assessment of patency in a single examination. In a series of 72 cases in which the presence of patency in at least one tube was proved, the hysterosalpingogram gave an accurate result in 83.3 per cent of cases, whereas the CO_2 test was correct in only 45.8 per cent. However, as these tests are complementary, both examinations should be carried out in all cases in which tubal patency is being assessed.

Venous intravasation occurred in only one patient in the present series of 535. The author considers that it is unlikely that the weakening of the uterine mucosa due to such conditions as trauma, excessive pressure of injection, and recent curettage, must still be regarded as important.

The therapeutic value of hysterosalpingography is uncertain. Various beneficial effects attributed to the injection of contrast material are described. It is difficult to prove the importance of any particular effect, and the occurrence of pregnancy in 34.4 per cent of the 93 patients does not justify the conclusion that hysterosalpingography has a specific therapeutic value. The psychologic effect may be of some significance.

THEODORE E. KEATS, M.D.
University of California, S. F.

THE GENITOURINARY SYSTEM

Hypaque, A New Urographic Medium: Preliminary Report on 300 Cases. Henry Bodner, Allan H. Howard, and Joseph H. Kaplan. J. Urol. **74**: 422–426, September 1955.

A relatively new contrast medium, Hypaque (sodium 3,5-diacetamido-2,4,6-triiodobenzoate) is compared with other contrast media from the standpoint of toxicity and diagnostic quality.

A 50 per cent solution of the new medium has a molecular iodine content of 59.87 per cent as compared with 66.5 per cent in a 70 per cent solution of Urokon. An acute toxicity study in animals revealed that in general the tolerance for Hypaque is higher than for Urokon or Diodrast. Hypaque produces no greater vein irritation than Urokon 30 per cent or Diodrast 35 per cent and is definitely less irritating than Urokon 70 per cent.

In a series of 300 consecutive cases studied with Hypaque, only 3.4 per cent of the films were classed as "poor." The percentage of diagnostic films was thus higher than with any of the contrast media with which comparison was made (Urokon 50 and 70 per cent, Diodrast 35 per cent, Neo-Iopax 50 per cent). There was also a definite decrease in the incidence of disagreeable reactions of all types.

From this study of a relatively small group of cases it would appear that Hypaque is a superior medium for excretory urography, but study of a larger series of cases over a longer period of time is recommended.

One illustration; 4 tables.

ROBERT L. MCDONALD, M.D.
University of Arkansas

An Assessment of Sodium Acetrizoate and an Experimental Basis for Its Use in Intravenous Pyelography. P. G. Keates. J. Fac. Radiologists **7:** 139–146, October 1955.

Sodium acetrizoate, marketed in the United States under the trade name Urokon and in Great Britain as Diaginol, is here compared with Diodone, which has two instead of three iodine atoms per molecule. The comparison included a study of the urine concentrations of the media at different intervals of time following intravenous injection. The findings established that the peak concentration of Urokon is five minutes earlier than that of Diodone, and that the concentration of Urokon falls off much more rapidly.

Because of the relatively slow fall in concentration with Diodone, the time of ureteric compression and radiography is not very critical. With Urokon, compression cannot be too long delayed. The advantage of the greater density of the medium must be seized during the six- to sixteen-minute period.

As the second part of this study, numerous pyelograms made with both media were reviewed by a panel of examiners. Without knowing beforehand which medium had been used, the panel members unanimously showed preference for the studies made with Urokon. The increased density of the medium made it particularly useful in cases where fluid restriction had been incomplete, where kidney concentrating power was impaired, or where obesity or overlying bowel contents tended to obscure kidney outlines.

Three roentgenograms; 2 graphs; 2 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Miokon. A Preliminary Clinical Report on a New Intravenous Urographic Medium. Charles H. Nicolai. Missouri Med. **52:** 703–704, September 1955.

Miokon (sodium diprotrizoate) was used for 750 intravenous urograms and 20 translumbar aortograms, and the results were analyzed to determine its toxicity and general usefulness. This medium contains 57.4 per cent iodine and is furnished in 30-c.c. ampules of 50 per cent strength. Animal and clinical experimental studies indicate a low incidence of untoward reactions.

Miokon was not used in persons with known allergies, and two test doses of 1 to 3 c.c. were administered prior to diagnostic injection. The incidence of reactions was lower if at least three minutes were taken for the injections.

Of the pyelograms, 96 per cent were considered satisfactory diagnostically. Nearly 600 of the 750 were graded as good to excellent. The incidence of mild side reactions was 9.8 per cent. One neuromuscular reaction occurred in a patient with a history of epilepsy and was readily controlled by barbiturate injection. The 20 translumbar aortographic studies were uneventful.

Two tables.

GEORGE A. SHIPMAN, M.D.
New Orleans, La.

Sodium Diatrizoate for Intravenous Pyelography. A Report of 100 Cases. Howard A. Hoffman, Stanley J. Koczera, Nelson L. Portnoy, Emery O. Lewis, Edward C. Vogt, and Wilson Simas. New England J. Med. **253:** 683–685, Oct. 20, 1955.

The authors report their experiences with sodium diatrizoate (Hypaque Sodium) as a contrast medium in 100 excretory urographic studies, including one *via* the intramuscular route in a child. The results are in accordance with previous reports lauding the increased rate of excretion of the medium, improved contrast in the films, and decrease in the number and severity of side-reactions.

Two roentgenograms; 2 tables.

SAUL SCHEFF, M.D.
Boston, Mass.

A Bacteriocidal Additive for Pyelographic Media. Russell B. Roth, Anthony F. Kaminsky, and Elmer Hess. J. Urol. **74:** 563–566, October 1955.

Certain limitations to the performance of retrograde pyelography have been imposed by the fact that, in spite of scrupulous technic, it may be possible to introduce bacteria into a previously unaffected portion of the urinary tract. Circumstances under which ordinary retrograde pyelography must be regarded as dangerous include all instances in which urinary tract infection is present and in which the status of the kidney or kidneys is unknown.

The authors report the performance of 219 pyelographic studies with the addition of a 2.5 per cent solution of neomycin sulfate to Skiodan, Diodrast, or Urokon. Neomycin sulfate has a marked bactericidal activity against the majority of gram-negative and gram-positive organisms ordinarily encountered in the urinary tract. This bactericidal additive has given rise to no recognizable toxicity or mucosal irritation. It is possible, by this method, to carry out retrograde pyelography in spite of urinary tract infections which might previously have been regarded as contraindications to this form of investigation.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

The Value of Chlor-Trimeton in the Prevention of Immediate Reactions to 70 Per Cent Urokon. Chester C. Winter. J. Urol. **74:** 416–421, September 1955.

The increased use of contrast media and the need for their employment in greater concentration necessitates redoubled efforts toward reducing the incidence and severity of reactions. There have been conflicting reports in the literature as to the value of antihistamine

preparations as prophylactic agents. In this study 900 patients were divided into two equal groups. One group received 25 c.c. of 70 per cent Urokon alone and the second group received the same medium mixed with 10 mg. of the antihistamine Chlor-Trimeton. Each group was further subdivided into individuals with and without an allergic background. Reactions were classified as (1) allergic, consisting of urticaria, asthma, dyspnea and sneezing; (2) neurovascular, consisting of pain, venous spasm, flushing, and dizziness; (3) psychogenic or cerebral, consisting of nausea and vomiting.

The total incidence of reactions in the group receiving Chlor-Trimeton was 17.7 per cent as compared to 31.1 per cent for the control group. The incidence of allergic reactions for the Chlor-Trimeton group was 3.7 per cent and for the control group 8.2 per cent. The incidence of psychogenic reactions was 10.2 per cent in those receiving Chlor-Trimeton as compared with 17.7 per cent for the controls. As would be expected, there was a definite increase in the number of allergic reactions in those individuals with an allergic history. The only severe reaction was in an individual of non-allergic background who received the Chlor-Trimeton-Urokon mixture. This was of the anaphylactoid type and resulted in no permanent damage.

From this study it would appear that Chlor-Trimeton is of definite value in reducing the incidence of true allergic reactions from 70 per cent Urokon.

Two tables.

ROBERT L. MCDONALD, M.D.
University of Arkansas

Agenesis of Abdominal Musculature with Ectopic Ureteral Orifice and Congenital Absence of Opposite Kidney and Ureter. Sam G. Jameson and James O. Cooper. J. Pediat. **47:** 489–495, October 1955.

The authors present a case of agenesis of the abdominal musculature, with ectopic ureteral orifice and congenital absence of the opposite kidney and ureter, to emphasize the importance of careful examination and observation for congenital anomalies in any child born of a diabetic mother. This is the twelfth recorded instance of ectopic ureteral opening into the seminal vesicle and, so far as the authors know, the first such case with congenital absence of the opposite kidney and ureter. Bilateral complete inguinal hernias, umbilical hernia, and herniation of the spleen into the subcutaneous tissue with each respiratory movement were observed on physical examination at birth. Despite absence of urinary symptoms, a complete urologic study was made as soon as the general condition of the infant permitted. Following urethroscopy, cystoscopy, and intravenous pyelography, a suprapubic cystostomy was performed, and an operative diagnosis of ectopic ureteral orifice was made. The postoperative course was uneventful, and follow-up studies revealed continued improvement of the right urinary tract. The patient was asymptomatic at the time of the report, some twenty months following operation.

The authors believe that all patients with a defect of the musculature of the abdominal wall should have complete urologic examination, regardless of the absence of symptoms, as there is a high probability that associated genitourinary anomalies may be present. Early examination, with prompt institution of corrective measures, may prevent irreparable damage to the urinary tract and permit normal function.

Five roentgenograms.

Primary Carcinoma of the Ureter. Eugene M. Savignac. Am. J. Roentgenol. **74:** 628–634, October 1955.

Primary carcinoma of the ureter is infrequent but no longer as rare as has been generally believed. A total of 333 cases have been recorded in the world literature (including the 3 new cases reported by this author), 137 of them in the past five years. Primary cancer of the ureter is a neoplasm of transitional epithelium and can possess all the features of tumors of the renal pelvis and the urinary bladder.

Seventy-five per cent of ureteral tumors are carcinomas, while 21 per cent are benign papillomas; the remaining 4 per cent consists of hemangiomas, sarcomas and fibromas. Papillary and solid types of carcinoma are of about equal frequency. The tumors may be multicentric and widely separated in the urinary tract. They may be pedunculated and occlude the lumen, sessile with invasion of the wall of the ureter, or diffuse papillary growths. Metastases are present in over 50 per cent of the cases.

A frequent clinical triad consists of hematuria, pain, and a palpable abdominal mass. A mass, which represents the distended hydronephrotic kidney, is present less often than the other findings of the triad. Bleeding occurs in nearly all cases. Pain may be due either to ureteral obstruction or to invasion of the ureteral wall. Surgery is the therapy of choice and preoperative and postoperative radiation appear to be of no value. The tumor is rarely found in patients under the age of twenty-five or thirty. It is most frequent in the sixth and seventh decades.

Intravenous pyelograms will show an enlarged kidney with diminished function or none at all, or may demonstrate a point of obstruction of the ureter, but generally a retrograde examination gives the most information. This may show complete obstruction or an irregular filling defect. The finding of an abrupt overhanging shelf formation, similar to that seen in carcinoma of the colon, permits a conclusive radiographic diagnosis.

Four roentgenograms.

DAMON D. BLAKE, M.D.
Bowman Gray School of Medicine

Ureteroceles in Children. Glen H. Gummess, Donald A. Charnock, Herman I. Riddell, and Charles M. Stewart. J. Urol. **74:** 331–335, September 1955.

Eleven cases of congenital ureterocele in children are reported, constituting about 2.7 per cent of all cases subjected to urological studies in the Los Angeles Children's Hospital in the course of a year. The essential etiologic factor is a stenosis of the ureteral meatus.

The diagnosis of ureterocele in childhood is difficult, but is possible in most instances. A complete physical examination sometimes reveals an abdominal mass either in the area of the bladder or the kidneys. Urinalysis frequently shows albuminuria and pyuria. The diagnosis depends, however, upon a complete urologic study. Excretory urography with well timed films will reveal a negative filling defect in the bladder early in the examination, which will later disappear. Associated tortuosity and dilatation of the ureters and pooling of the contrast medium may be shown. Cystograms will frequently demonstrate a filling defect in the bladder. Cystoscopy should also be done.

Treatment consists in relief of the obstruction and

correction of secondary complications. A plea is made for accurate urological study and operative treatment prior to use of multiple courses of antimicrobials, "in an effort to preserve a few drugs that may be used effectively in the later care of these patients."

Six roentgenograms; 4 tables.

WALTER L. SIMS, M.D.
University of Arkansas

TECHNIC

Xeroradiography. I. Apparatus and Method of Use. W. D. Oliphant. Brit. J. Radiol. **28:** 543–544, October 1955.

II. The Present Medical Applications. T. H. Hills, R. W. Stanford, and R. D. Moore. Ibid., pp. 545–551.

In 1937 Chester F. Carlson described and patented a new photographic technic which was based entirely on physical processing. This new method of image reproduction depended upon electrostatic and triboelectricity. In view of the essentially dry nature of the process it was called xerography.

The xerographic plate consists essentially of a mechanically rigid backing plate, which must possess a certain amount of electrical conductivity, on one surface of which is deposited uniformly a film of amorphous selenium 50 to 100 micra thick. Prior to sensitization, this plate is quite unaffected by light, by x-rays, or by radiation from radioactive substances. The plate is charged by exposing the top surface in the dark to the corona discharge from a suitably shaped electrode. The surface film is charged to a potential of 400 to 500 volts.

A sensitized plate must be kept in a cassette fitted with an x-ray-transparent dark slide, but it is handled in precisely the same manner as an x-ray film during exposure. When the exposure has been completed, the charge distribution remaining on the plate constitutes a latent electrostatic image. As this image is invisible, it is necessary to carry out a "development" process. The process, known as the powder cloud method, makes use of the fact that, when powder particles are whirled into a cloud, the individual particles are charged, and the powder will adhere more or less in proportion to the radiation which has fallen on the charged plate.

Once the image has been developed, it may be examined, photographed, or projected onto a screen, or the powder may be transferred to a suitable adhesive paper. When all of the information has been abstracted, the remaining powder may be wiped carefully off the surface of the plate and the plate used again.

Hills, Stanford, and Moore describe the medical applications of xeroradiography. Three factors affect the detail of the xeroradiograph, namely the time for which the plate is charged, the x-ray exposure, and the time for which the exposed plate is subjected to the powder cloud. For any given subject, the optimum combination of these factors must be determined. When this has been done for a thin bone such as a metacarpal, the results approximate those obtained with non-screen films. With a thicker bone, as the femur, the xeroradiograph suffers little, if any, in comparison with a screen film. In general, the evidence suggests that the plates are some two and a half times slower than standard non-screen film and ten times slower than screen film.

A series of comparisons was made covering the skull, jaws, the cervical, dorsal, and lumbar spine, shoulder, lung, hip, knee, ankle, foot, fingers, and wrist, and some of the films are reproduced.

The present application of xeroradiography in medicine is limited primarily by the exposure needed. For this reason the practical use of the method is restricted to radiography of the peripheries. Both bone detail and soft tissue are well demonstrated provided care is taken to avoid distortion.

As to the advantages of the method, it is pointed out that the apparatus employed requires no more electrical energy than that needed by a 100-watt lamp; no darkroom, chemicals, or water are needed, the only expendable item being the powder, which is used at a very slow rate. The entire process of charging and developing the plate requires less than a minute, and the finished picture is available for inspection in about half a minute after exposure.

Fourteen xeroradiographs; 5 conventional roentgenograms.

J. P. CHAMPION, M.D.
Grand Rapids, Mich.

Microradiography. I. Microradiography: A Review. A. Engström, S. Bellman, and Bengt Engfeldt. Brit. J. Radiol. **28:** 517–532, October 1955.

II. Projection Microradiography. W. C. Nixon and V. E. Cosslett. Ibid., pp. 532–536.

III. A Sealed-off X-ray Tube for Contact-Microradiography. B. Combée, J. Houtman, and A. Recourt. Ibid., pp. 537–542.

The first of this group of papers is devoted to a review of the subject of microradiography, opening with a brief history, an account of the physical principles and factors involved, and a description of some of the equipment used. There follows a discussion of unique applications of this procedure in the study of histology, cell physiology, and pathology.

By soft-tissue microradiography one can calculate the weight per unit area of the various structures in the specimen. Thus it has been possible to study the weight of the axon and the myelin sheath in a single nerve fiber. By means of microradiographic technic much has been learned, also, concerning deposition and resorption of bone in both normal and abnormal states, the development of dental tissues, and the nature of some of the pathological processes involving them.

Another purpose to which microradiography has been applied is the study *in vivo* of the uptake of certain radioactive isotopes. In compact bone it has been shown that the uptake of isotopes is localized to subperiosteal and endosteal areas and to certain osteons.

Microangiography, or the demonstration of microscopic blood vessels which are rendered opaque by suitable materials, has been used to study ovarian circulation in rabbits and vascular reactions in frostbite. The lack of uniformity of vascular reaction thus demonstrated in various portions of the damaged tissue, could not have been discovered by vital microscopy because of the smallness of field size.

The use of microdiffraction to study the stucture of biological materials has been very successful. The technical factors concerned with this phase of microradiography are discussed, and a brief history of its development is presented. The rapid development of new x-ray sources of high specific intensity and new types of microcameras will widen this field. Now it is possible to attack many problems in biology and medicine by using the equipment which is commercially available.

Numerous microradiograms illustrate the applications described above.

Projection microradiography, the subject of the second paper, is a recent development, differing from earlier methods in that the specimen and the photographic plate are separated until an enlarged x-ray image is obtained. The degree of magnification is the ratio of the distances of film to ray source and specimen to x-ray source. A special x-ray tube for this purpose is described. Direct x-ray enlargements up to ×1000 have been obtained and some subsequent photographic enlargement is possible. Illustrations demonstrating the use of projection microradiography in the field of biology, medicine, and metallurgy are reproduced.

Contact microradiography, used for the study of sections of plants and animals, requires very soft x-rays because of the thinness of the objects. Since it has been possible to obtain these only by the use of x-ray tube windows of thin metal foil, which are not vacuum-tight, the tubes hitherto employed have had to be continuously evacuated. This resulted in a high cost of operation and an elaborate and complicated apparatus.

Combée and his associates have now constructed a sealed-off x-ray tube for contact microradiography which they designate C.M.R. 5.

The construction is such that the geometrical blurring by the focal spot (300 micra), for an object of 10 micra thickness in contact with a 5 micra thick maximum resolution emulsion, is 0.2 micron on the front and 0.3 micron at the back of the emulsion. This degree of blurring can be neglected because the resolution of the film is no better than 1 micron. The quality of the x-ray beam with the tube in operation at 3 kv. is described.

The requirements for an ideal photographic emulsion for microradiographic work are outlined and a hope is expressed that manufacturers of emulsions will strive to reach this goal.

Four illustrations demonstrating the use of contact microradiography in medicine, biology and quality control in paper manufacture are included. Several other applications are suggested.

H. C. JONES, M.D.
Grand Rapids, Mich.

Experimental Colour Radiography. A. Bryce. Brit. J. Radiol. **28:** 552–553, October 1955.

This paper opens with a brief history of the relatively little that has been done with color in radiography. The author has tried direct color radiography by exposing three-emulsion color printing paper to x-rays. Without intensifying screens a blue image is produced. A back blue-fluorescing intensifying screen results in a purple image with the grain of the paper base superimposed upon it. A front intensifying screen alone in contact with the blue sensitive emulsion results in a yellow-to-brown image, depending upon the exposure. If the emulsion is exposed to colored light during development, a two-color radiograph is produced. A brown color is present in the area of heavy x-ray exposure, while a cyan image is found where there has been no x-ray exposure, and varying shades of green and brown at the intermediate exposures.

So far only color printing paper rather than film has been used, because of the cost. Color film, however, will be tried in the future, so that a direct comparison between monochrome and color radiographs can be made. It is pointed out that a color-film method must compare favorably with the conventional approach in exposure speed and latitude, definition, ease and speed of processing, and, of course, cost, if it is to be used other than experimentally.

J. A. GUNN, M.D.
Grand Rapids, Mich.

High kV Radiography and Enlargement Technic. K. P. Mody. Indian J. Radiol. **9:** 139–142, August 1955.

The author reviews the subject of high-voltage radiography editorially, briefly outlining the basic principles and the development of the method. He states that, "in a general way it may be said that by adding 10 kv for voltages up to 75 and 15 kv for voltages higher than 75 the exposure time is cut down to half." The advantages of the reduced exposure time for the elimination of voluntary and involuntary movements is obvious. Other considerations are the smaller amount of radiation received by the patient and the decrease in heat generation in the tube, thereby prolonging its life. Though the contrast on the film may appear less striking than with low-voltage technics, actually there is a gradation of opacity due to different densities in the tissues. The technic has been found particularly useful in chest roentgenography and is well adapted to gastrointestinal and gallbladder examinations and to studies of the lumbar spine and the pregnant abdomen.

A direct enlargement technic employing high-voltage radiography is briefly described. This, the author believes, offers some advantages in simplifying the reading of suspicious shadows within the chest, the mucosal pattern in the stomach, and early pathological changes in the bones.

NEIL E. CROW, M.D.
University of Arkansas

Percutaneous Splenic Portograms in Dogs: Technique and Examples of Usefulness. Robert E. Davis, George A. Hallenbeck, Frank R. Lichtenheld, and John H. Grindlay. Surgery **38:** 708–711, October 1955.

It is considerably more difficult to inject percutaneously into the slender mobile spleen of the dog than into the human spleen for study of the portal circulation. The authors describe a surgical method in which the dog's spleen is partially explanted into subcutaneous tissues and fixed, becoming permanently accessible for direct injection, without alteration of position or vascular relationships of its major portion. This procedure was carried out in 8 dogs and provided reliable information on the topography and functional status of the portal and splenic veins.

Three roentgenograms.

Reduplication of Radiographs. Editorial. Elliott C. Lasser and Edmund J. Owczarzak. Am. J. Surg. **90:** 545–546, October 1955.

It is often helpful to have a duplicate roentgenogram to send to another physician, for teaching and other purposes. Roentgenograms can be duplicated by contact printing, photographic duplication, reproduction by the reversal process, solarization, and illuminization. The first four of these methods are discussed briefly. The illuminization process, which the authors believe has definite advantages, is described in detail. No special equipment is needed, and satisfactory duplicates can be produced in a matter of minutes. Results are excelled only by photographic duplication of the originals. The entire process can be carried out in normal indoor lighting and need not interfere with the routine operation of the darkroom.

RADIOTHERAPY

The Palliation of Bronchial Carcinoma by Radiotherapy. Gerald Blanshard. Lancet 2: 897–901, Oct. 29, 1955.

The effects of palliative x-ray therapy in 35 patients with histologically proved bronchial carcinoma are analyzed.

Relief of symptoms was afforded as follows:

	Cases Improved
Chest pain	
Mediastinal (3 cases)	3
Visceral (6 cases)	4
Invasive (4 cases)	0
Cough (25 cases)	19
Dysphagia (4 cases)	3
Dyspnea (24 cases)	14
Hemoptysis (13 cases)	7
Vena caval obstruction (6 cases)	5

General improvement was demonstrated in 21 patients, including 8 of 15 with squamous-cell carcinoma and 13 of 20 with oat-cell and other histologic types of growth; this suggests that the latter are more radiosensitive than the former. Seventeen of the patients were able to lead an independent life subsequent to treatment, and 6 returned to work.

Of 12 patients with constitutional disturbance (malaise, lassitude, sweats, and fever) associated with bronchial infection, 4 given antibiotics and radiotherapy improved; of 8 who received radiotherapy alone, only 5 improved.

In 17 cases in which radiological correlation with symptomatic relief was possible, radiological regression was seen in 13; in the other 4 the condition remained stationary or became worse.

Response to therapy was slightly better in upper-lobe growths than in lower-lobe tumors. The most effective course was found to be an average dose of 2,161 r given in twelve treatments. Higher dosage and more prolonged treatment was found to produce no better effects.

Six illustrative case histories are presented.

Ten roentgenograms; 4 tables.

The Place of Radiation Therapy and of Surgery in the Treatment of Uterine Cancer. H. L. Kottmeier. J. Obst. & Gynaec. Brit. Emp. 62: 737–751, October 1955.

The author discusses the entire problem of the place of radiation therapy and of surgery in the treatment of uterine cancer. This discussion is a lengthy one and does not lend itself well to abstracting. It should be read in its entirety by those interested in this important question.

At the Radiumhemmet (Stockholm), from which the report comes, a radiotherapy procedure for cervical carcinoma has evolved along the following lines: (1) A careful examination including cystoscopy, urography, and sometimes phlebography.

(2) Usually, a fractionated intracavitary radium treatment as the first step of the irradiation. The treatment is individualized in regard to the degree of infection, the gross anatomic type of the tumor, its spread to paracervical or paravaginal tissue and the area of the obturator fossa. Due regard is paid to the dosage distribution both from the intra-uterine and the vaginal radium. Several types of intra-uterine and vaginal applicators are used.

(3) Roentgen therapy to the parametrium and the pelvic wall in all cases, and in selected cases also to the paravaginal tissue through perineal fields.

(4) Injection of radioactive colloidal gold into the parametrium in selected cases of suspicious lymph node metastases.

(5) Additional treatment with telecobalt in selected cases of cancer of the cervix with pelvic lymph node metastases as far as these can be diagnosed by phlebography, urography, and clinical examination.

A direct comparison of radiation therapy and radical surgery in operable cases of carcinoma of the cervix is possible only if all cases applying to an institution are recorded according to the international classification and then assigned within each stage in strict correlation with one or the other method of therapy. In reviewing the results from leading institutions the author concludes that the five-year results obtained by radiotherapy are definitely better than those reported for surgery. He feels that surgery is useful, however, in cases which fail to respond to radiotherapy, which recur, or which can be shown by some reliable method to have small chance of being radiocurable. He believes, further, that radiation therapy can destroy cancer in the regional lymph nodes in some patients and that "radiotherapy offers a chance at least as good as surgery to cure cases with lymph node metastases."

In carcinoma of the body of the uterus, physicians at the Radiumhemmet have applied radiological treatment according to the packing method plus operation most often in those cases where primary radiotherapy has failed.

The application of a central radium source or a tandem is considered adequate only for the early case when the uterine cavity is not grossly enlarged. Otherwise such a radium application does not fulfill the requirements of a curative treatment. An attempt to deliver a homogeneous dose to all parts of the uterine cavity, irrespective of its size and shape, was introduced in 1936 at the Radiumhemmet by packing the uterine cavity with multiple uniform radium containers. This procedure has proved satisfactory and has been used in some 2,300 cases. Additional radium should always be applied in the vagina. This treatment must be individualized with regard to the site of the growth and the presence of vaginal metastases. Supplementary roentgen therapy should be given in inoperable cases, in cases in which the uterine cavity is difficult to fill, and in cases involving both corpus and endocervix.

In the patient presenting a cancer of the corpus with no contraindication to major surgery, a total hysterectomy and removal of the adnexa is considered an adequate type of procedure.

At the Radiumhemmet, the use of radium as a prophylactic postoperative procedure has been advocated in corpus carcinoma. A dose of 2,000 gamma r is administered to the wall of the vagina. Additional roentgen therapy is given in cases in which it is doubtful if radical surgery has been carried out.

The question that must be answered by physicians who treat carcinoma of the uterus is not the question of surgery *versus* radiotherapy. "It is rather the question of under which circumstances surgery and

under which circumstances radiotherapy is the treatment of choice in the individual patient."

Two photomicrographs; 2 drawings; 1 chart; 11 tables.

THEODORE E. KEATS, M.D.
University of California, S. F.

Clinical Experiences with Wilms' Tumors. Michael J. Feeney, Ralph B. Mullenix, Robert J. Prentiss, and James M. Whisenand. J. Urol. **74:** 301–311, September 1955.

The authors report 14 cases of Wilms' tumor. Three patients had bilateral tumors, and another underwent two additional operations to remove new masses in the retroperitoneal space.

The cases are summarized in table form. One patient was alive fifteen years after surgery, free of neoplasm, but with polycystic renal disease. Another was alive and well five years following nephrectomy and a third was alive after seven years, though new tumors had twice been excised since initial surgery. Two patients had been followed less than one year, and the remaining 9 died of the tumor.

The authors stress four cardinal points necessary to improve the usually gloomy prognosis. These are:

1. Early diagnosis, best made by accurate abdominal palpation.
2. Prompt nephrectomy with a generous exposure, permitting initial ligation at the pedicle and wide excision of the renal envelopes.
3. Postoperative x-ray therapy.
4. Careful, regular, and prolonged abdominal reexaminations with immediate removal of any newly discovered retroperitoneal masses.

All of the patients in this series received postoperative roentgen therapy and 10 were irradiated preoperatively as well, but no information as to dosage is given.

Seven roentgenograms; 11 photographs and photomicrographs.

JAMES R. MORRISON, M.D.
University of Arkansas

Polycythemia Vera Terminating in Acute Leukemia. Report of a Case and Review of Literature. Norman Skversky, Theodore H. Mendell, and Abraham M. Frumin. Arch. Int. Med. **96:** 565–566, October 1955.

Thirty-four cases of polycythemia vera terminating in acute leukemia have been recorded in the literature. All were of the granulocytic variety. The authors add another, also granulocytic, in a 65-year-old woman who was known to have had polycythemia for twelve years. Two patients were treated solely with venesections; the others received varying courses of x-rays, P^{32}, and venesection.

While it would seem that acute leukemia may well represent the end-stage of some cases of polycythemia vera, the possibility of internal radiation (P^{32}) or external radiation (x-ray) accelerating this process cannot be disregarded. The authors' patient received 61 mc. of P^{32} over an eleven-year period; the total amount of x-irradiation is unknown.

Preliminary Experiences with a 50 Gram Converging Beam Radium Unit. Douglas Quick and Jeanne Delano Richmond. Am. J. Roentgenol. **74:** 635–649, October 1955.

The authors report a two-and-one-half year experience with a 50-gram converging-beam radium unit designed for the Roosevelt Hospital, New York, under the supervision of Dr. Failla. It contains twenty-five 2-gram radium capsules evenly distributed in a 30-cm. ring. With the multiple beams focused at a depth of 10 cm. below the skin surface, output is in the order of 3 gamma roentgens per minute. The slow rate of administration is believed to be of considerable advantage in the treatment of chronically ill and debilitated patients with advanced carcinoma. The size and shape of the beam provide the advantage of greatly increased depth doses, with only a limited volume of normal tissue irradiation. The authors report that normal tissue changes in the immediate field of irradiation are much less than with conventional high-voltage roentgen radiation and believe that bone repair after adequate tumor dosage is possible because of the lesser damaging effect of gamma radiation in bone. This lesser effect of gamma radiation on soft tissues and bone accounts for the less severe depressing influence on normal blood-forming mechanisms. Transfusions have seldom been required in the patients treated.

The impression has been gained that a number of the more resistant types of malignant growth (such as cancer of the mouth and upper mucous membrane tract, bladder, prostate, and inoperable lung tumors) are now being more influenced by the better quality of radiation and in increasing degree.

The authors have long felt that the rather universally accepted average curative dose of 6,000 r is too low. They are achieving considerably higher doses without prohibitive reaction in the uninvolved surrounding tissues.

The detailed description of the unit and of certain cases treated cannot be adequately abstracted.

The unique isodose patterns achieved with this unit are illustrated.

Twenty-five roentgenograms; 4 photographs; 2 isodose curves.

G. BROGDON, M.D.
Bowman Gray School of Medicine

A Radon Applicator for Treating Carcinoma of the Vocal Cord. C. C. J. Minty and D. F. Robertson. J. Fac. Radiologists **7:** 136–138, October 1955.

A single rigid polythene holder for radium or radon needles made particularly for use as an applicator for vocal cord carcinomas is described in this article. The unit is designed to fit under the thyroid cartilage through a fenestration. When stitched into place, it holds all sources immobile in whatever geometrical pattern is desired.

The use of radon is suggested, inasmuch as the sources are active to their ends and permit more latitude in the event that unsymmetrical distribution of activity might be desired. Two cases in which the method was used are described.

Three roentgenograms; 1 photograph; 1 diagram.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

A Method of Dose Calculation with Applications to Moving-Field Therapy. B. M. Wheatley. Brit. J. Radiol. **28:** 566–573, October 1955.

The distribution of radiation dose in a patient can only rarely be measured. It is also manifestly impossible to produce a complete set of data covering all clinically useful combinations of fields employed in treatment, because of the large number of variables.

The irradiation dose varies with the co-ordinates of the point within the body and with the four physical parameters (quality, F.S.D., field area, and field shape) of the irradiating beam. It is common practice to prepare isodose charts for one or two principal planes, but these charts do not contain data appropriate for irregular fields or for the variety of conditions which occur when moving beams are used.

Because of the obvious inconveniences listed above, the author describes simple numerical methods of calculating the dose at various points in a single field and shows how the methods can be extended for multiple fields and the dose problems of rotation technics. For details, the original paper must be consulted.

Five figures; 4 tables. H. C. JONES, M.D.
Grand Rapids, Mich.

RADIOISOTOPES

The Diagnostic Value of Protein-Bound Iodine and Forty-Eight Hour Protein-Bound I^{131} as Indices of Thyroid Disorders. K. H. Clarke, Edna V. Sherriff, and Dora Winikoff. M. J. Australia **2:** 89–90, July 16, 1955.

A four-year project at the University of Melbourne on the diagnostic value of protein-bound iodine (P.B.I.) revealed it to be the best single index for distinguishing between hyperthyroidism, euthyroidism, and hypothyroidism. The best physical index studied was the level of protein-bound radioiodine forty-eight hours after a tracer dose of I^{131} (forty-eight-hour $P.B.I^{131}$). The latter, however, does not separate hypothyroidism from other thyroid disorders.

Since determination of P.B.I. is a complicated procedure and that of forty-eight-hour $P.B.I^{131}$ is relatively simple, it was hoped that the latter would be an adequate index of hyperthyroidism. The authors determined both values in 100 cases with no known influencing medication. The P.B.I. measures the level of circulating hormone, while the forty-eight-hour $P.B.I.^{131}$ is related to the rate of iodine turnover in the body. Consequently a high value of $P.B.I.^{131}$ may be due either to thyroid hyperactivity or to the release of hormone into the blood stream in cases of iodine starvation in euthyroid or hypothyroid patients. This is supported by the authors' observation that a low value for $P.B.I.^{131}$ is usually associated with euthyroidism while high values do not exclude this possibility. It is felt, therefore, that the number of P.B.I. determinations can be reduced, since a low forty-eight-hour $P.B.I.^{131}$ index can be accepted as adequate evidence of euthyroidism. If, however, this index is high, a P.B.I. will be necessary to determine if hyperthyroidism is present. The authors regard this combined procedure as being 89 per cent accurate.

Two graphs; 3 tables.

GEORGE A. SHIPMAN, M.D.
New Orleans, La.

Cancer of the Thyroid Gland: Our Experience with Radioactive Iodine. P. E. Russo and H. H. Mathews. South. M. J. **48:** 937–940, September 1955.

Since the Isotope Clinic at the University Hospitals, Oklahoma City, Okla., was established in 1949, 41 cases of cancer of the thyroid have been seen and studied. There were 13 males and 28 females in the series. The average age was forty-eight; most of the patients were over fifty, but 2 were under ten years of age.

The present report is concerned primarily with 13 patients who were treated with radioiodine. All had had previous surgery, and 6 had had x-ray therapy. These cases fall into three groups: (1) In 2 cases (15 per cent) I^{131} uptake by the tumor was high, producing subjective and objective improvement. Favorable control of the disease occurred and results were gratifying. (2) In 4 cases (30 per cent) I^{131} uptake by the tumor was slight but the patients experienced some temporary improvement. However, the course of the disease and the outcome were not appreciably altered. (3) In 7 cases the tumor showed no selectivity in I^{131} pick-up and no favorable response to this form of treatment resulted.

At the time of the report, 6 of the 13 patients were dead, 3 of them not surviving over eighteen months. All but 1 of the 7 patients still alive have evidence of existing disease; 2 have survived twenty-six and twenty-one years respectively following surgery. In 2 cases the original microscopic diagnosis was benign disease, but several years later proved bone metastases occurred.

In the authors' opinion, surgery with or without external irradiation still remains the treatment of choice in the great majority of thyroid cancers. A small percentage, probably about 15 per cent, will show an avidity for radioiodine and in such instances this form of treatment gives excellent results. In patients in whom neither further surgery nor external irradiation is advisable, radioiodine should be tried for palliative purposes.

Three cases presenting unusual features are reported in detail.

The Thyrotoxic Remnant. John H. Nodine, William H. Perloff, Theodore E. Sopp, Ricardo N. Ferrandis, and Danilo de Albuquerque. Am. J. M. Sc. **230:** 397–407, October 1955.

The authors studied 6 patients who, following treatment with radioiodine or surgery for thyrotoxicosis, were clinically euthyroid or hypothyroid but in whom the I^{131} upake and/or the $P.B.I.^{131}$ remained high. The reasons for these discrepancies are not completely clear, but certain possibilities seem likely. An elevated I^{131} conversion rate in the patient who is clinically euthyroid or even frankly myxedematous may be related to the low amounts of hormonal iodine stored in the thyroid glands of these individuals. The failure of correlation of the thyroidal fraction of I^{131} (that present in the gland as well as the amount already secreted into the blood stream as hormonal radioiodine) and the serum protein-bound iodine level and clinical status are more difficult to understand. Several possible explanations are offered, the most likely of which is a reduced serum iodide level, which would tend to decrease the absolute amount of iodine available to the trapping mechanism of the thyroid gland.

Eight graphs; 4 tables.

HOWARD J. BARNHARD, M.D.
University of Arkansas

Sporadic Cretinism with Goiter. A. J. Aballí, F. Costales, and Z. Prendes. Rev. cubana de pediat. **27:** 513–530, September 1955. (In Spanish)

Four cases of sporadic cretinism with goiter, 3 of

them in siblings, are presented. In all of them uptake of I^{131} by the thyroid was very high. In 2 cases the goiter was visible, and in the other 2 it was palpable. Although this type of cretinism is rather rare, it is possible that many more cases will be detected in the future with routine determinations of I^{131} uptake by the thyroid in all varieties of hypothyroidism.

From a review of the literature, it is evident that there are two different subgroups of this form of cretinism: one in which the thyroid is unable to convert inorganic iodine to diiodotyrosine and the other due to failure to transform diiodotyrosine into thyroxine.

JAMES T. CASE, M.D.
Santa Barbara, Calif.

Study of the Hepato-Biliary Metabolism of Thyroid Hormones in Man with the Aid of I^{131}. B. R. Scazziga, T. H. Béraud, and A. Vannotti. Schweiz. med. Wchnschr. **85**: 1019–1021, Oct. 15, 1955. (In French)

The authors investigated the hepato-biliary metabolism of thyroid hormone after administration of I^{131}, by studying the plasma chromatographically. Recent work has shown the important role of the liver in regulating the metabolism of the thyroid hormone. Albert (J. Clin. Endocrinol. **12**: 942, 1952) has demonstrated an entero-hepatic circulation of the hormone. It is resorbed by the intestinal wall, as is shown by analysis of the portal blood, is re-excreted by the liver, and is carried by the bile into the stools. A glucuronic conjugate is the principal form that thyroxin takes as it is eliminated from the liver. Animal experiments show that this compound is found in the plasma after the common duct has been ligated, but not in normal animals. The importance of the liver in thyroid hormone regulation also receives clinical support: an increase in protein-bound iodine is found in epidemic hepatitis.

The authors confirm the experimental findings that the glucuroconjugate of thyroid hormone is not found normally in the plasma, that there is an entero-hepatic circulation of thyroxine, and that these substances are elevated in patients with mechanical icterus. However, only 1 patient had an elevation with viral hepatitis. This would indicate that the conjugation of the thyroid hormone is a function of the liver cell.

Three figures.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Influence of Estrogen and Progesterone on Radioactive Iodine Uptake by Rat Thyroid. F. A. Soliman and E. P. Reineke. Am. J. Physiol. **183**: 63–66, October 1955.

Physiological doses of estrogen and progesterone were injected into ovariectomized rats, alone or in combination, in the sequence believed to occur during the estrous cycle. Forty-eight hours after injection of the steroid hormone, the effect on thyroid function was measured by determining the six-hour uptake of I^{131} by the thyroid.

A single injection of either 6 or 300 R.U. estradiol benzoate significantly increased I^{131} uptake. The concurrent administration of 0.4 or 0.8 mg. progesterone reduced the uptake by estrogen-treated rats down to or slightly below the level observed in ovariectomized controls. Progesterone in doses of 0.2 or 0.4 mg. also reduced uptake slightly; 0.8 mg. caused a slight increase.

In rats which had undergone both ovariectomy and hypophysectomy, estrogen had no effect on I^{131} uptake, indicating that a functional pituitary is necessary for the effect on thyroid function to be expressed. Progesterone produced no significant change in I^{131} uptake.

On the basis of these results, the authors suggest that the previously observed variations in thyroid function during the estrous cycle of the rat may be explained by changes in balance of the ovarian hormones—estrogen and progesterone.

Two tables.

Effect of Hormones on Renal Clearance of Radioiodine in the Rat. Jaime Paris, Elizabeth Ford, Nona Lorenz, F. Raymond Keating, Jr., and A. Albert. Am. J. Physiol. **183**: 163–166, October 1955.

The renal clearance of radioiodine was assessed in intact, thyroidectomized, hypophysectomized, adrenalectomized, and adrenalectomized-hypophysectomized rats before and after treatment with a variety of hormone preparations. Under standard conditions of fluid and electrolyte intake, adrenalectomy reduced the clearance to one-half and hypophysectomy or combined ablation of the pituitary and adrenal glands to one-fourth the normal value. Cortisone acetate fully restored clearance values to normal in the adrenalectomized rat, but only to two-thirds that of normal in the hypophysectomized-adrenalectomized animals. The combination of cortisone acetate and extracts of whole pituitary or cortisone and growth hormone restored the clearance of hypophysectomized-adrenalectomized rats to normal levels. Pituitary extract alone or growth hormone alone exerted only moderate restorative action. Intact rats showed a slight depression of radioiodine renal clearance following the acute or chronic administration of cortisone acetate and showed no change after desoxycorticosterone acetate. The depression of thyroidal uptake of I^{131} in the cortisone-treated normal rat cannot be ascribed to a concomitant increased clearance of radioiodide.

Two tables.

Radio-Active Isotopes in the Treatment of Bladder Tumors. D. M. T. Cones. South African M. J. **29**: 915–919, Sept. 24, 1955.

The value of the various radioisotopes in the treatment of tumors of the bladder is discussed, and 3 cases are presented.

Benign papillomatosis may be treated by the injection of a solution of radioactive gold through a closed catheter. This procedure is considered to be particularly satisfactory because of the ease of administration of the isotope and the lack of postirradiation symptoms.

For malignant neoplasms of the bladder, the chief value of isotopes lies in the possibility of irradiating the entire mucosal surface. When a radioactive gold solution is used in such cases, it must be combined with some form of more deeply penetrating radiation, as from an intracavitary radiocobalt source.

For intracavitary radiocobalt therapy, a catheter has been designed in which a solid cobalt source is mounted in the center of an intravesical balloon. Not only does this method avoid the risk of a burst balloon associated with liquid isotopes, but is has certain advantages over radium, as the compactness of the source, equality of isodose distribution, and ease with which the position of the cobalt can be changed under radiographic control.

Although the number of cases treated by these methods is limited, it is believed that the results

obtained are encouraging and that continued use of the procedures is warranted.

Four roentgenograms; 1 photomicrograph; 2 photographs.

Further Results Obtained in the Treatment of Cancer of the Cervix: A Progress Report. Willard M. Allen, Alfred I. Sherman, and A. Norman Arneson. Am. J. Obst. & Gynec. **70:** 786–790, October 1955.

One year previously the authors reported the results obtained in patients treated by radiogold and compared them with those obtained with x-rays and radium over a four-year period, 1950–53 (Am. J. Obst. & Gynec. **68:** 1433, 1954. Abst. in Radiology **65:** 647, 1955). The present report covers the same patients, plus those treated during 1954.

Again, no conclusions are reached beyond the observation that, seemingly, results have been better in patients treated with radiogold than in patients treated during the same period with x-rays and radium or in patients treated prior to this study with x-rays and radium.

Considering all the cases, it appears that the results (six months to five and a half years) are as good in patients treated with radiogold and radium but without surgery as in those in whom treatment was completed by radical Wertheim hysterectomy and pelvic lymphadenectomy. In many instances, however, insufficient time has passed to judge the effectiveness of treatment. While good results have been obtained with radiogold and surgery, it cannot be assumed that radium is unnecessary, since many of these cases were of Stage I.

Eight tables. ROBERT L. EGAN, M.D.
University of Texas, Houston

Surgery and Radioactive Gold Treatment for Carcinoma of the Ovary. Roland S. Cron, Irving I. Cowan, Russel L. Gorthey, and Frank G. Karioris. Am. J. Obst. & Gynec. **70:** 910–916, October 1955.

This is a preliminary report on the clinical results of prophylactic and palliative use of radiogold in 28 cases of ovarian carcinoma treated in 1952–55. While the addition of radiogold to the conventional treatment was not shown to have any marked therapeutic advantage, it exercised a definite deterrent effect upon the production of ascites. Of 17 patients with serous cystadenocarcinoma and 6 with adenocarcinoma, 15 required tapping before gold was administered, while only 5 needed subsequent paracentesis. The patients did not experience significant distress from the treatment. The dosage of the intraperitoneal gold ranged from 100 to 225 mc. The average is 160 mc in a single injection in 200 c.c. of saline.

The authors point out that any evaluation of radiogold as a therapeutic agent on the basis of this study is impossible, since the patients selected for its use were chiefly those with ascites, which is an indication of highly malignant, widespread disease.

Six tables. ROBERT L. EGAN, M.D.
University of Texas, Houston

The Use of Radioactive Gold in the Treatment of Effusion Due to Carcinomatosis of the Pleura and Peritoneum. Morton M. Kligerman and David V. Habif. Am. J. Roentgenol. **74:** 651–656, October 1955.

This paper presents a clinical evaluation of the effects of radioactive gold administered intraperitoneally and intrapleurally, as a palliative agent, in 35 patients with fluid collections secondary to carcinomatous implants. The principal aim is to repress fluid formation so that thoracentesis or paracentesis is either no longer necessary or is required less frequently. The study covers an eighteen-month interval, and includes 22 injections into the pleural space on 20 different patients, 14 cases of carcinomatous ascites, and 2 cases of non-malignant obstructive ascites. [One patient was treated for fluid in both chest and abdomen.]

The method of administration is described. For pleural effusions the dose ranged between 21 and 47 mc, the usual dose being 35 mc where no loculation was suspected. Most patients with ascites received approximately 100 mc, with a range of 50 to 120 mc. The length of time over which no further removal of fluid was required was used as an index of efficacy of treatment. If fluid recurred in less than one month, treatment was rated as a failure. If tapping was not required for one to two months, the result was considered fair. A good result was represented by those cases in which further tapping was not required for two months or more after the instillation of gold. Occasionally, there was a latent period of two or three weeks between the time of instillation of gold and evidence of benefit.

Of the 20 pleural cases with 22 areas treated, 12 showed a good result and 2 a fair result. Of the 14 intraperitoneal instillations for malignant ascites, 8 gave a good result, 1 a fair result. The treatment was without effect in the 2 non-malignant cases.

Side-effects were minimal in both incidence and severity. In one patient in whom 47 mc was instilled, a sterile pleuritis resulted, lasting for about six days.

Eight of the 16 patients treated for ascites experienced some radiation sickness of one to six days duration, characterized by lassitude, anorexia, nausea, and in some instances vomiting. In 2 patients symptoms suggesting a chemical peritonitis occurred.

Three tables. I. MESCHAN, M.D.
Bowman Gray School of Medicine

Treatment of Malignant Serous Effusions with Radioactive Colloidal Chromic Phosphate. Henry L. Jaffe. Am. J. Roentgenol. **74:** 657–666, October 1955.

The author reports an evaluation of the results of the use of radioactive colloidal chromic phosphate in the treatment of malignant serous effusions in 50 patients followed for six months to three years.

Some radiation hazards and practical problems connected with the intraperitoneal and intrapleural use of radiogold prompted the author to search for an equally effective agent which would have a longer physical half-life and thus be easier to keep in supply, would produce pure beta radiation and thus require less unwieldy lead shielding for protection and therefore cost less to ship by air freight, and could be injected on an out-patient basis with Atomic Energy Commission approval, at less cost of administration.

It was found that when the soluble form of phosphorus (P^{32}) is converted into the colloidal suspension of chromic phosphate, the radioactive phosphorus retains its radiation characteristics as though it were in the soluble form.

The author presents tables comparing radioactive colloidal gold (Au^{98}) and radioactive colloidal chromic phosphate (P^{32}) both in respect to radiation characteristics and practical aspects. The chromic phosphate offers many practical advantages as well as a greater versatility in patient care.

The palliative results were considered to compare favorably with those reported with radiogold. Improvement was obtained in 66 per cent of 30 patients with advanced carcinoma receiving intrapleural injections and in 60 per cent of 20 patients given intraperitoneal injections.

In view of these results the authors feel that radioactive colloidal chromic phosphate is far superior to radiogold, since it has all the advantages and none of the disadvantages.

A new closed-cartridge system syringe for administration of the radioactive phosphate is described.

Thirteen illustrations, including 2 roentgenograms; 4 tables.

J. F. MARTIN, M.D.
Bowman Gray School of Medicine

Radioactive-Source Corrections for Bremsstrahlung and Scatter. S. J. Wyard. Nucleonics **13:** 44–45, July 1955.

Simple formulae are presented for the estimation of the intensity and the spectral distribution of bremsstrahlung due to both beta rays and mono-energetic electrons. Though the intensity of the bremsstrahlung is usually very small compared with the intensity of the primary gamma rays from an isotope source, knowledge of its magnitude is sometimes important. A convenient table is presented which gives the spectral distribution of the bremsstrahlung produced by beta rays of a given maximum energy, and also by mono-energetic electrons of a given energy. The ratio of the intensity of scattered radiation to that of primary radiation is also treated briefly, and a method of approximation is given. The spectral distribution of the scattered radiation is plotted for a point source of gamma rays located at the center of a sphere and also at the center of a cylinder. Applications of these approximations are illustrated for a few different radioactive isotopes, and a second table gives the relative intensity of bremsstrahlung produced in both solid and liquid sources. A calculation of the relative dose rate produced by primary gammas and by scattered radiation from a radium tube is also included.

Two figures; 1 table.

JOHN S. LAUGHLIN, PH.D.
Memorial Center, New York

Inability to Assess Absorption of Iron from Plasma Radioiron Curves. T. H. Bothwell, Barbara Mallett, R. Oliver, and Mary D. Smith. Brit. J. Haematol. **1:** 352–357, October 1955.

Following administration of oral iron, there is prompt rise in plasma iron. It has been assumed by many that there is a relationship between the level to which plasma iron is raised and the actual quantity absorbed. Recent findings have resulted in some doubt as to the validity of this assumption, particularly since the character of tolerance curves depends not only on amount absorbed but also on the rate of absorption and rate of removal of iron from the plasma. The authors used radioactive iron to determine if a more accurate index of iron absorption could be obtained from the amount appearing in plasma if corrections were made for the rate of removal of iron. The corrected figures of absorption were compared with those obtained by estimating quantity of unabsorbed radioactivity in feces in 10 ambulant patients with non-obstructing, non-bleeding peptic ulcer.

Results showed variation in total absorption of radioiron from 5.4 to 44.0 per cent of the oral dose. The absorption was highest during the first hour. After a maximum level had been reached, there was in most cases a decline at an exponential rate, suggesting no further absorption. In a few, absorption continued, and in 1 a new peak was reached.

When the results for absorption of iron as calculated from plasma radioiron curves were compared with those obtained from the quantity of unabsorbed radioactivity present in the feces, good agreement was present in 5 cases, but in the remaining 5 large discrepancies occurred, with plasma radioiron data giving lower figures for absorption in each case.

The authors conclude that the amount of radioactivity appearing in plasma is not a reliable quantitative measure of iron absorption.

Two graphs; 1 table.

GEORGE A. SHIPMAN, M.D.
New Orleans, La.

Training of Residents in Radioisotope Techniques. Donald S. Childs, Jr. J.A.M.A. **159:** 541–544, Oct. 8, 1955.

The three-month formal radioisotope training of fellows in radiology at the Mayo Foundation consists of three phases.

Theoretical principles, covering basic mathematics, units of matter, radioactivity, physical properties of radiation, biological effects, of radiation, radiological safety, theory and use of measuring instruments, radiological units, dosimetry, and tracer methodology, are presented by means of lectures, demonstrations, and reading. Logarithms, exponents, statistics, and the slide rule are explained. Films produced by the Army Signal Corps and the Atomic Energy Commission are useful for this part of the program.

Practical applications carried out by the residents include identification of radioisotopes, calibration and use of radioisotopes, calibration and use of measuring devices, preparation of radioactive material for assay, *in vivo* and *in vitro* radioisotope assay, autoradiography, safety procedures, radiation surveys, decontamination, waste disposal, and bookkeeping.

Clinical aspects of the training include the medical work-up of cases, indications for the use of isotopes, post-treatment care, and the evaluation of results.

Weekly discussions are devoted to current problems and a review of recent publications.

Should the resident desire to carry out a research project, facilities are available for such work.

RICHARD E. BUENGER, M.D.
Chicago, Ill.

RADIATION EFFECTS; PROTECTION

Radiation Nephritis. Burton J. Grossman. J. Pediat. **47:** 424–433, October 1955.

The author reports a case of radiation nephritis in an infant. The child was admitted to the hospital at nine months of age, with an elevated temperature and a diagnosis of bronchitis. During the course of the physical examination, a large mass was found in the left side of the abdomen. Intravenous pyelography, on

April 24, 1954, revealed a mass in the left perirenal area displacing the left kidney anteriorly and the left ureter medially. The calyceal system was not well visualized on the left. The right calyceal system and ureter appeared normal and excreted the contrast medium well. A left nephrectomy was performed on April 26; the histologic diagnosis was Wilms' tumor of the left kidney, of the tubular cystic and papillary cystic adenocarcinomatous type. Preoperatively irradiation was given over the upper abdomen in the region of the left kidney, for a 1,000 r depth dose, through 10 x 10-cm. portals anteriorly and posteriorly. On the third postoperative day, irradiation was begun to a lower thoracic and upper abdominal bridge (15 x 20 cm.). X-ray therapy was interrupted for six days because of melena, but by May 19, 2,000 r had been administered to the bridge area.

The patient was discharged from the hospital on May 28, but he became progressively anemic and was readmitted on Aug. 31. Urinalysis revealed albuminuria, hyaline and granular casts, and occasional white blood cells. The blood pressure ranged from 170 to 180 systolic, and 120 to 140 diastolic. The course was steadily downhill, and death occurred after a generalized major convulsion on Sept. 17.

Autopsy led to a diagnosis of radiation nephritis; postirradiation changes of the left adrenal, stomach, proximal jejunum, lungs, left lobe of the liver, and pancreas; uremia with widespread recent hemorrhages, most extensive in the atrophic left lobe of the liver, pancreas, stomach, jejunum, and left adrenal. There was no evidence of recurrence of the Wilms' tumor.

One table.

Carcinoma of the Skin Appearing 49 Years After a Single Diagnostic Roentgen Exposure. Report of a Case. J. S. Mitchell and J. L. Haybittle. Acta radiol. **44:** 345–350, October 1955.

The authors report a case of carcinoma of the skin appearing forty-nine years after a single large diagnostic exposure to roentgen radiation. This they believe is the longest latent period recorded in the literature up to the present time.

A woman, aged 70, had received a diagnostic roentgen examination for renal calculi in 1898. The exposure, over the right upper abdomen, was said to have lasted for about an hour. A blistering skin reaction appeared about two weeks after the roentgen exposure but subsequently healed. However, in the summer of 1947, ulceration appeared below the right costal margin anteriorly and gradually extended. The lesion measured 7.5 x 5 x 1 cm., the edge was raised, and most of the surface ulcerated. There was an area of surrounding atrophic skin measuring 13 x 12 cm., with numerous telangiectases and small areas of patchy pigmentation. The biopsy specimen revealed extensive squamous-cell carcinoma.

The patient was in poor general condition and surgery was not possible. Radiotherapy was attempted and a total dose of approximately 3,000 r on the skin was delivered in an overall time of thirty-nine days. A favorable response ensued and it was concluded that this lesion was at least as radiosensitive as most examples of squamous-cell carcinoma of the skin of similar size and histology. The lesion, however, did not heal and the patient died on May 23, 1949.

It is impossible to estimate accurately the dose which this patient received in 1898, but it was thought that the kilovoltage used was probably about 100 kvp at a skin-target distance of about 20 cm. On this basis, it seems likely that the skin dose, including back-scatter, may have been 1,500 r at the site of the lesion. It is unlikely that the dose exceeded 2,000 r.

A somewhat parallel case was reported by Rübe (Strahlentherapie **94:** 239, 1954. Abst. in Radiology **64:** 477, 1955).

Three photomicrographs; 1 photograph; 1 table.

I. MESCHAN, M.D.
Bowman Gray School of Medicine

Comparison of the Sensitiveness and Consistency of Certain Blood Tests for Persons Exposed to Minor Degrees of Ionizing Radiation. D. O. Shiels. M. J. Australia **2:** 91–93, July 16, 1955.

The Factory Department of the Australian Ministry of Labour and National Service has stated that the total and differential white cell counts offer the earliest means of detecting the biological effects of absorbed radiation. The author presents evidence to show that there are other more sensitive indicators. He recommends: (1) the ratio of large lymphocytes plus monocytes to small lymphocytes; (2) the ratio of large to small lymphocytes; (3) the percentage of lymphocytes which have granules in the cytoplasm; (4) the percentage of monocytes of a particular type, which he designates without description as "B type." Each of these values was determined on samples of blood from 6 persons prior to exposure to radiation and again after a period of four to seven months exposure. The exposures were estimated to be less than 20 per cent of the tolerance dose (0.3 r per week, free air dose). The ratios mentioned were both significantly raised, the percentage of lymphocytes with granules was diminished, and there was an increase of type B monocytes. A change of over 30 per cent for the factors mentioned was observed in almost all cases, but 6 subjects is a small number upon which to base conclusions.

Two figures; 3 tables.

GEORGE A. SHIPMAN, M.D.
New Orleans, La.

Acute Toxicity of Radon. Donald A. Morken. Arch. Ind. Health **12:** 435–438, October 1955.

The inhalation and retention of radon and its decay products constitute an important health hazard in the uranium mining industry. Until recently radon alone was considered to be the hazard, but measurements in uranium mines have shown that the concentration of the short-lived decay products of radon may well exceed the concentration of radon itself, especially in well ventilated mines.

A search of the literature disclosed no record of an inhalation experiment which determined unequivocally the toxicity of radon or its decay products as separate entities. In order to clarify, and possibly amplify, the data on both acute and chronic exposures, the author has carried out a series of investigations.

Adult mice (strain CAF_1) were placed in a chamber with a closed respiration system and exposed to concentrations of radon of about 0.22 mc per liter, free of decay products, for periods up to forty hours. The doses ranged from 1.1 to 8.8 mc-hr. per liter. Control mice were kept in the chamber for ten hours, with no radon present.

Mice exposed to radon free of decay products exhibited all the gross toxic symptoms previously re-

ported in experiments in which decay products were present. The LD 50 of the mice exposed to pure radon was found to be lower than any value previously recorded (this difference is probably attributable to the technic employed in earlier experiments), lying between 5.7 and 8.8 mc-hr. per liter. Anemia was less marked than after an x-ray exposure of comparable lethality.

Measurements of air activity indicated that atmospheres of radon essentially free of decay products may be produced.

Preliminary data are included on the shortening of life span produced by exposure to radon in the range of 1.1 to 8.8 mc-hr. per liter.

Two figures; 2 tables.

The Combined Effects of Thermal Burns and Whole-Body X-Irradiation: III. Study of Blood Coagulation. W. M. Davis, A. K. Davis, W. Lee, and E. L. Alpen. Ann. Surg. **142**: 66–75, July 1955.

In two previous studies the combined effect of thermal burns and total-body x-irradiation was reported. The first dealt with the effect of the combined injury on survival time and mortality (Alpen and Sheline: Ann. Surg. **140**: 113, 1954. Abst. in Radiology **64**: 795, 1955) the second with the influence of the osmotic and mechanical fragility of rat erythrocytes on the observed increase in mortality (Alpen, Alexander, and Davis: Am. J. Physiol. **179**: 541, 1954. Abst. in Radiology **65**: 651, 1955). The present study is devoted to blood coagulation in rats subjected to high-intensity radiant-energy thermal burns, total-body x-irradiation, and a combination of the two. The burns were applied to the sides and backs of the animals; irradiation was at 250 kv, h.v.l. 1.5 mm. Cu. Included are observations of the modified Lee-White (silicone) clotting time, heparin clotting time, blood platelet concentration, and prothrombin time.

A dose of 500 r total-body x-radiation without burns produced a rapidly developing thrombocytopenia and defective clotting mechanisms, as measured by Lee-White and heparin clotting times. At 100 r, a brief thrombocytosis was followed by mild, transient thrombocytopenia, as reflected in changes in both the Lee-White and heparin clotting times.

High-intensity radiant energy thermal burns produced a brief fall in the level of circulating platelets, followed by a sustained thrombocytosis.

The combined effects of thermal burns and total-body x-radiation consisted of the same initial fall in platelets seen with burns alone, followed by the same degree of thrombocytopenia occurring in animals receiving total body x-irradiation at the particular dose given. No significant differences were observed in animals given the radiation only and in those in which burns and radiation were combined, except that the coagulation defect was less severe in the animals receiving both injuries.

It is apparent that the observed defective coagulation mechanism fails to account for increased mortality in animals receiving total body x-irradiation combined with thermal burns. From a clinical point of view, however, the thrombocytopenia and defective clotting mechanism do permit recognition of casualties in which thermal burns or other traumata are complicated by superimposed total body irradiation, and the degree of thrombocytopenia is correlated with the radiation dose.

Twelve graphs; 2 tables.

Studies on Susceptibility to Infection Following Ionizing Radiation. III. Susceptibility of the Intestinal Tract to Oral Inoculation with Pseudomonas aeruginosa. Carolyn W. Hammond, David Ruml, Dorothy B. Cooper, and C. Phillip Miller. J. Exper. Med. **102**: 403–411, Oct. 1, 1955.

A striking difference, observed in previous experiments, between normal and irradiated mice in their response to administration of *Pseudomonas aeruginosa* seemed to warrant a study of the fate of this microorganism after its introduction into the gastrointestinal tract. Mice were accordingly inoculated with *Pseudomonas* (by means of a curved tube attached to a small tuberculin syringe) on the fifth day postirradiation (550 r) and killed at daily intervals thereafter to determine the numbers of these bacteria in the small and large intestine. It was found that the bacteria were much more likely to become implanted and to multiply in the intestine, particularly the small intestine, of the irradiated than of the normal mouse, with the difference most apparent on the third day following inoculation.

Attempts were then made to explain the underlying mechanisms responsible for this effect of x-radiation. Neither variation in *p*H of gastric or duodenal contents, propulsive motility of the intestinal tract, nor the ability of the intestinal contents to support the growth of *Pseudomonas in vitro* served, however, to elucidate this difference. It is believed that an explanation may lie partially in some recent experiments on the effect of fasting on resistance to infection, in which unirradiated mice deprived of food for twenty-four hours before or after inoculation retained *Pseudomonas* in almost as great numbers as did non-fasting irradiated mice; these preliminary results are considered to be of sufficient interest to warrant further investigation.

One graph; 1 table.

Studies on Susceptibility to Infection Following Ionizing Radiation. IV. The Pathogenesis of the Endogenous Bacteremias in Mice. Lee E. Gordon, David Ruml, Helen Jo Hahne, and C. Phillip Miller. J. Exper. Med. **102**: 413–424, Oct. 1, 1955.

The authors attempted to determine why the onset of fatal bacteremia in mice is delayed for so long after moderate doses of total body x-irradiation and by what route the causative microorganisms gain entrance to the blood stream. It has been observed that the period of maximal damage to the intestinal mucosa does not correlate in time with the period of incidence of bacteremia caused by microorganisms of intestinal origin. The former takes place within a few hours after exposure, and repair is completed by the fourth or fifth day; not until the latter part of the first post-irradiation week, however, do the bacteremias begin to occur.

In this study, mice were killed each day postirradiation and cultures were made of the tissues and fluids through which bacteria must pass on their way from the intestine to the blood stream. These included mesenteric lymph nodes, mesenteric lymph, liver, and portal blood. Systemic blood was also cultured, as well as one of its most important filters, the spleen. The bacteremias are always caused by members of the mouse's enteric flora; in the first of the series of experiments reported, a nonpathogenic microorganism, *Serratia marcescens*, was introduced into the gastrointestinal tract and maintained there by feeding it to the mice in their drinking water.

It was found that in half of the normal mice examined, cultures of mesenteric lymph nodes were positive for enteric bacteria, and in almost as many for *Serratia marcescens*. It was concluded that bacteria in small numbers were able to pass from the lumen of the unirradiated intestine as far as the regional lymph nodes. Except for the pathogen *Salmonella*, such bacteria were rarely found in liver or spleen, and never in the blood of the normal animals.

After x-irradiation with 700 r, the incidence of positive cultures showed the liver or spleen to be infected with enteric microorganisms before the blood stream was invaded. It appears, therefore, that these elements of the reticuloendothelial system were able for a time to maintain the sterility of the blood after failure of the more immediate defenses against bacterial invasion from the intestinal tract. The fatal bacteremias which develop in mice following exposure to moderate doses of x-radiation are not primarily the result of radiation injury to the intestinal mucosa but rather of the impairment of the animals' defenses against its own enteric bacteria. It is concluded that, if any increased migration of bacteria through the intestinal mucosa resulted from the radiation injury, the increase must have occurred very soon after irradiation.

Two graphs; 1 table.

Effect of Repetitive Exposures to Gamma Rays on the Hematopoietic System of the Rat. Siegmund J. Baum, Donald J. Kimeldorf, and Elly M. Jacobsen. Blood **10**: 926–932, September 1955.

The authors have conducted a well organized and well controlled study of the effect of multiple exposures to gamma rays on the hematopoietic system of the rat. The animals received 75 r gamma whole-body irradiation exposures, and groups were sacrificed after one to eight weeks. Hematologic examinations were made following the last exposure in each group.

The hematologic effects observed showed little change from group to group, and the maximum changes occurred at approximately the same time following the last exposure regardless of the number of previous exposures. These results were ascribed to the capacity of the hematopoietic system to recover completely, or almost completely, during the seven-day interval between exposures. There was no evidence of an increasing sensitivity or increasing resistance of the hematopoietic system following multiple low dosage gamma irradiation over a period of eight weeks.

Two graphs; 1 table. JAMES W. BUICE, M.D.
University of Arkansas

Effects of High-Energy Particles, X-Rays, and Aging on Lens Epithelium. L. von Sallmann, C. A. Tobias, H. O. Anger, C. Welch, S. F. Kimura, C. M. Munoz, and A. Drungis. Arch. Ophth. **54**: 489–514, October 1955.

Evidence is presented which bears upon three aspects of the problem of radiation-induced cataracts: the location of the radiosensitive epithelial cells, the damage of which might be the chief causative factor in the formation of radiation cataract; the relative biologic effectiveness of radiations with different linear energy transfers; the morphology of cell damage in the lens epithelium caused by the various radiations and the damage produced by old age.

Selective exposure of the equatorial and the central area of the rabbit lens to the deuteron beam confirmed the impression of high radiosensitivity of cells in the germinative zone—"the mitotic area"—of the epithelium in contrast to the relative radioresistance of cells in the large central part.

Other experiments on rabbits with densely ionizing radiations (alpha particles and deuterons) and x-rays failed to show any significant difference in the effects of the two types of radiation on cell division (onset, delay, and over-compensating increase), but injury produced in the cell nuclei by isodoses of high-energy radiations greatly exceeded that of x-rays.

The relative biological effectiveness of x-rays *vs.* alpha particles for this radiation effect was statistically calculated as 4.1, varying from 2.7 to 6.1 at a confidence range of 99 per cent. The relative biological effectiveness of x-rays *vs.* deuterons was calculated as 3.9 and varied from 2.3 to 6.6 at the same confidence range. The effects of alpha particles and deuterons were of similar magnitude.

Long-term observations of a brief series indicated that, following bombardment of the equatorial zone or of the entire lens with the same dose, in reps, of high-energy particles, the latent period between exposure and initial cataractous changes is much shorter than that following roentgen irradiation.

As in other tissues, the earliest radiation-induced morphological changes, observed at the twenty-minute interval, consist of chromatin bridges in anaphase and telophase of cells which had entered the mitotic cycle at the time of exposure. Extrusion of chromatin material from the cell nucleus often leads to the death of the cell. On the other hand, cells in which this sign of damage is less extensive may survive. Depletion of the cell population by death of the cells and failure in the differentiation of damaged cells seems to play a part in the eventual development of radiation cataract.

The cell degeneration caused by alpha particles and deuterons differs quantitatively but not qualitatively from that caused by x-radiation. Studies on age-induced cell degeneration in the lens epithelium of rats revealed a striking resemblance between the cytopathology of this cell layer in old age and that of lenses exposed to ionizing radiations.

A statistical analysis of data on the effects of alpha particles, deuterons, and x-radiation is appended.

Thirty-six figures; 10 tables.

Adrenal Ascorbic Acid and Histological Changes in Male and Female Rats After Half-Body X-Ray Irradiation. Bernard C. Wexler, Richard Pencharz, and Sydney F. Thomas. Am. J. Physiol. **183**: 71–74, October 1955.

X-irradiation (625 r) of rats with the entire sagittal half of the body of each animal protected by a lead shield was found to cause much greater depletion and more active repletion of adrenal ascorbic acid than total-body irradiation. The intensity of this response was more acute in the male. Although adrenal glands removed from a lead-shielded body-half were heavier and contained higher levels of ascorbic acid, the contralateral unprotected glands underwent qualitatively similar ascorbic acid changes as well as histologic alterations. No severe untoward symptoms, such as diarrhea or morbidity, were observed. Histologically, the tinctorial, physical characteristics and zonal distribution of lipids indicated very active cortical discharge immediately following exposure, culminating in exhaustion.

It is postulated that half-body irradiation is less noxious symptomatically and stimulates a greater degree of adrenal reactivity than total-body irradiation, since certain humoral and glandular elements (with emphasis on components belonging to the pituitary-adrenal axis) may be afforded protection by a lead shield.

Two illustrations; 1 table.

The Effect of Radiation on the Nucleic Acid, Nitrogen, and Water Content of the Yoshida Sarcoma. Joseph W. Gardella and Eleanor J. Lichtler. Cancer Res. **15**: 529–531, September 1955.

Studies are reported in which measurements of cell volume and average cell content of ribonucleic (RNA) and desoxyribonucleic (DNA) acid, nitrogen, and water were made in the Yoshida rat sarcoma before and at intervals up to forty-eight hours after exposure to 1,000 r x-radiation *in vivo*.

A marked and simultaneous increase in the mean cell volume, RNA, nitrogen, and water content of the tumor cell was encountered from seventeen to twenty-four hours after exposure. The increase in RNA and nitrogen content per cell was roughly proportional to the increase in cell water, so that the concentration of RNA and nitrogen was not appreciably altered in the irradiated cell. This suggests that x-radiation does not seriously disturb the metabolism of RNA and nitrogen and that cell growth, in terms of these parameters at least, continues unimpaired.

The metabolism of DNA, on the other hand, appeared to be markedly impaired by irradiation, since the content of DNA per average tumor cell fails to increase concomitantly with the other constituents measured. To this extent, the biochemical mechanisms of the nucleus appear to be paralyzed and, by inference, nuclear division obstructed so that continued cytoplasmic growth in the absence of cell division results in the formation of large cells, at least in some instances.

These data indicate further that radiation in the range of 1,000 r does not increase the permeability of the cell to water. The fairly proportionate increase in RNA and nitrogen and cell water observed after irradiation suggests rather that the accumulation of water within the irradiated cell is probably the result of continued and orderly cytoplasmic growth in the absence of cell division.

One photomicrograph; 3 tables.

Studies on *Trichinella spiralis*. III. Effect on the Intestinal Phase of Trichinosis of Feeding Massive Numbers of Irradiated Trichina Larvae. IV. Effect of Feeding Irradiated Trichinella Larvae on Production of Immunity to Re-Infection. V. Tests for a Strain of Trichina Larvae Resistant to Radiation. S. E. Gould, H. J. Gomberg, F. H. Bethell, J. B. Villella, and C. S. Hertz. Am. J. Path. **31**: 933–963, September–October 1955.

The papers listed above are included in a series of five experimental studies of *Trichinella spiralis* infestation.

III. White rats fed 12,000 non-irradiated excysted larvae of *T. spiralis* (48 to 60 larvae per gm. of body weight) died, apparently mainly as a result of the intestinal phase of the infection. Feeding of the same number of larvae that had been exposed to 10,000 r merely caused transient diarrhea in some animals. The feeding of 12,000 larvae or of 24,000 larvae that had been exposed to 18,000 r generally (in 19 of 20) caused no diarrhea and permitted the animals to gain weight steadily. In all rats fed irradiated larvae (10,000 r or 18,000 r), the parasites were lost rapidly from the intestinal tract.

On this basis it is inferred that, if a person were to eat raw or undercooked, heavily trichinosed pork that had been irradiated in all parts with at least 18,000 r, he would suffer little or no ill effect from irritation of the intestine by the larvae, and that the parasites would disappear rapidly from the intestinal tract.

IV. Rats fed larvae of *T. spiralis* that had been irradiated with 10,000 r (a dose that does not prevent the larvae from developing into adult forms but does result in partial or complete sexual sterilization of the adult worms) were found to have a definite degree of immunity to re-infection with non-irradiated larvae. If the dose of irradiation was increased to 18,000 r (a dose that prevents most larvae from maturing to adult forms), little or no immunity resulted.

V. The possibility has been suggested that exposure of *Trichina* larvae to gamma radiation might result in selective survival of those which were relatively radioresistant and that this might conceivably lead to a radioresistant race. Larvae were exposed to doses of 10,000 r (which cause sexual sterilization of most of the developing adult worms) and 18,000 r (which inhibit development to adult forms). It was found that these doses did not induce in the irradiated larvae the property of radioresistance, and there was no evidence that the progeny of those capable of reproduction became a radioresistant strain.

In all of the studies the source of radiation was Co^{60}.

Six photographs.

Effect of X-Irradiation on Glucose Absorption. H. M. Dickson. Am. J. Physiol. **182**: 477–478, September 1955.

Irradiation reduces the intestinal absorption of carbohydrate as well as of other substances. It appeared possible that this might be due to a decrease in gastric evacuation, limiting the supply of carbohydrate available, or to a reduction in the concentration of hexokinase following irradiation, since phosphorylation of hexokinase has been postulated as the crucial reaction in the active absorption of glucose.

The author measured the intestinal absorption of glucose in mice four hours after irradiation, a time at which gastric emptying is known to be reduced to approximately 60 per cent of normal. This was followed by absorption studies four hours and seventy-two hours after irradiation, using loops of small intestine to eliminate the possible retarding influence of the stomach. Finally, *in vitro* tests of hexokinase activity of small intestine of normal and irradiated mice were carried out.

Despite the marked reduction in gastric emptying, with a resulting reduction in the quantity of sugar supplied to the intestine, the amount of glucose absorbed per hour was not affected by irradiation. This observation was confirmed by the studies on intestinal loops. Homogenates of small intestine taken from irradiated animals showed no impairment of hexokinase activity. Thus the observed decrease in the absorption rate of glucose cannot be ascribed to retarded gastric evacuation, nor can it be attributed to a decrease in the hexokinase activity of the intestines. The effect of x-rays may be directly on the intrinsic permeability of the intestinal mucosa.

X-Irradiation in Hamsters, and Effects of Streptomycin and Marrow-Spleen Homogenate Treatment. Willie W. Smith, Robert Q. Marston, Leon Gonshery, Ilo M. Alderman, and H. Jeanette Ruth. Am. J. Physiol. **183**: 98–110, October 1955.

Because x-irradiated hamsters respond favorably both to streptomycin and to bone marrow injection they can be used to study effects of radiation doses which would otherwise cause death from infection, hemorrhage, or anemia, and for comparing effects of the two treatments after single or multiple exposures to radiation.

The irradiation LD 50 (twenty-eight days) of hamsters was found to be increased by streptomycin to 800 r from a control value of 700 r, and by an intracardial injection of marrow-spleen homogenate to approximately 1,080 r. The effect of homogenate on survival showed up earlier than the effect of streptomycin. Streptomycin given for only the first three days did not improve survival and it was as effective when started on the third as on the first day after irradiation. Animals receiving between 1,400 and 10,000 r survived four to six days. Neither streptomycin nor homogenate alone prolonged survival at 1,400 r but the two treatments in combination did have this effect. The combined treatments did not consistently increase survival following doses of 1,050 to 1,160 r above that obtained with homogenate alone.

Leukocyte counts in severely irradiated hamsters (LD 90) treated with streptomycin began to return to normal about seven days following exposure, and in those treated with homogenate after about five days. In the latter essentially no anemia developed. A sharp weight loss occurred at this time in the animals not treated with homogenate.

Bacteria were isolated from the heart blood of a majority of the untreated hamsters that died after exposure to 550 to 1,160 r. The presence of *Pseudomonas* was associated with the shortest, and negative cultures with the longest survival times. Streptomycin was more effective in reducing the incidence of positive cultures than in reducing mortality. Homogenate treatment increased resistance to experimental infection with *Proteus* or *Paracolon* seven days after irradiation. The intestinal epithelium showed severe damage but little actual denudation the third day after exposure to 1,000 r. On the fifth day there was extensive regeneration of the intestinal epithelium in these animals but no regeneration was seen following exposures to 2,000–4,000 r. Submucosal hemorrhage was extensive. Most of the animals exhibited evidence of bacterial invasion on the fifth but not on the third day following irradiation. Streptomycin increased survival in hamsters exposed at intervals of two weeks to 450 r (twice) but not to 400 r (three times) although in the latter case bacteremia and its reduction by streptomycin were the same as in littermates exposed once to 800 r. In animals exposed five to seven times to 300 r the incidence of positive cultures was low and streptomycin was without effect. Leukocyte recovery failed after the second exposure to 550 r or the third exposure to 400 r, but moderately good levels were maintained through seven exposures to 300 r.

Eight figures; 6 tables.

Protection of Personnel During Roentgenological Examinations. Vincent W. Archer. Am. J. Roentgenol. **74**: 667–673, October 1955.

This paper is concerned with the problem of leukemia in radiologists and the possible role of exposure of the circulating blood to radiation as well as of the blood-forming organs. He divides general methods of protection into two main categories; (1) reducing the amount of secondary radiation; (2) protection of the fluoroscopist by appropriate measures.

The use of relatively small shutter openings during fluoroscopy is of considerable importance, since there is about twenty times as much scatter at the edge of the table when the shutters are wide as when they are opened moderately. The taking of spot films is considered to add significantly to exposure of the fluoroscopist, and the Bucky aperture at the side of the table is also a source of secondary radiation, which can be reduced by narrowing or covering. The top of the fluoroscopic tube cone should be as close as possible to the under surface of the table, and two or three millimeters of aluminum is recommended as tube filtration. The importance of being aware of the tube excitation time during fluoroscopy is stressed.

The fluoroscopy gown of spun lead glass fabric designed by the author represents an attempt at more complete protection of the body from secondary radiation. He recommends individual radiation monitoring before such a gown is ordered, since working conditions and habits determine the protection requirements for various parts of the body. These requirements can be met by varying the number of layers of the fabric.

Several charts and tables are presented, showing per cent transmission through lead glass fabric at various kilovoltages, dosage to various parts of the body during fluoroscopy, and radiation received by patients during different examinations. DAMON D. BLAKE, M.D.
Bowman Gray School of Medicine

The Protective Effect of Cysteamine Against Roentgen Ray Injury on Ears of Rabbits Irradiated Under Conditions of Complete Anoxia. Francis Lothe and Finn Devik. Acta radiol. **44**: 306–312, October 1955.

Many hypotheses have been suggested to explain the well known protective effort of sulfhydryl compounds against various forms of roentgen-ray damage. Some suggest an association between the action of SH-compounds and the concentration of oxygen. This possibility was examined by observing whether or not these compounds have any protective effect when irradiation is carried out under conditions characterized by a complete lack of oxygen.

The ears of anesthetized rabbits were irradiated under conditions of complete anoxia, achieved by perfusing the ear with an oxygen-free solution in an atmosphere of nitrogen. One ear of each rabbit was used as a test object and the other as a control. Single doses of approximately 5,000 r, 8,000 r, and 12,000 r, were administered.

Six rabbits were treated under conditions of anoxia and a protective effect was observed in comparison with the control. Six rabbits received cysteamine (introduced in perfused blood) in the presence of oxygen, with results suggesting a protective effect of the cysteamine against the roentgen damage to the oxygenated ear. Twelve rabbits were used to determine the effect of complete anoxia plus cysteamine. A concentration of 100 mg. per cent cysteamine was used in 6, and 6 received 30 mg. per cent. Cysteamine appeared to give slight additional protection when administered to ears irradiated in the anoxic state, indicating that cysteamine and anoxia, at least to some

degree, act along different paths in the radiobiologic process.

Three photographs; 1 table

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Preparatory Experiment on Protection of Skin Against Irradiation Damage. P. Gersholowitz, M. Weidersheim, and R. D. Tucker. South African M. J. **29**: 846–847, Sept. 3, 1955.

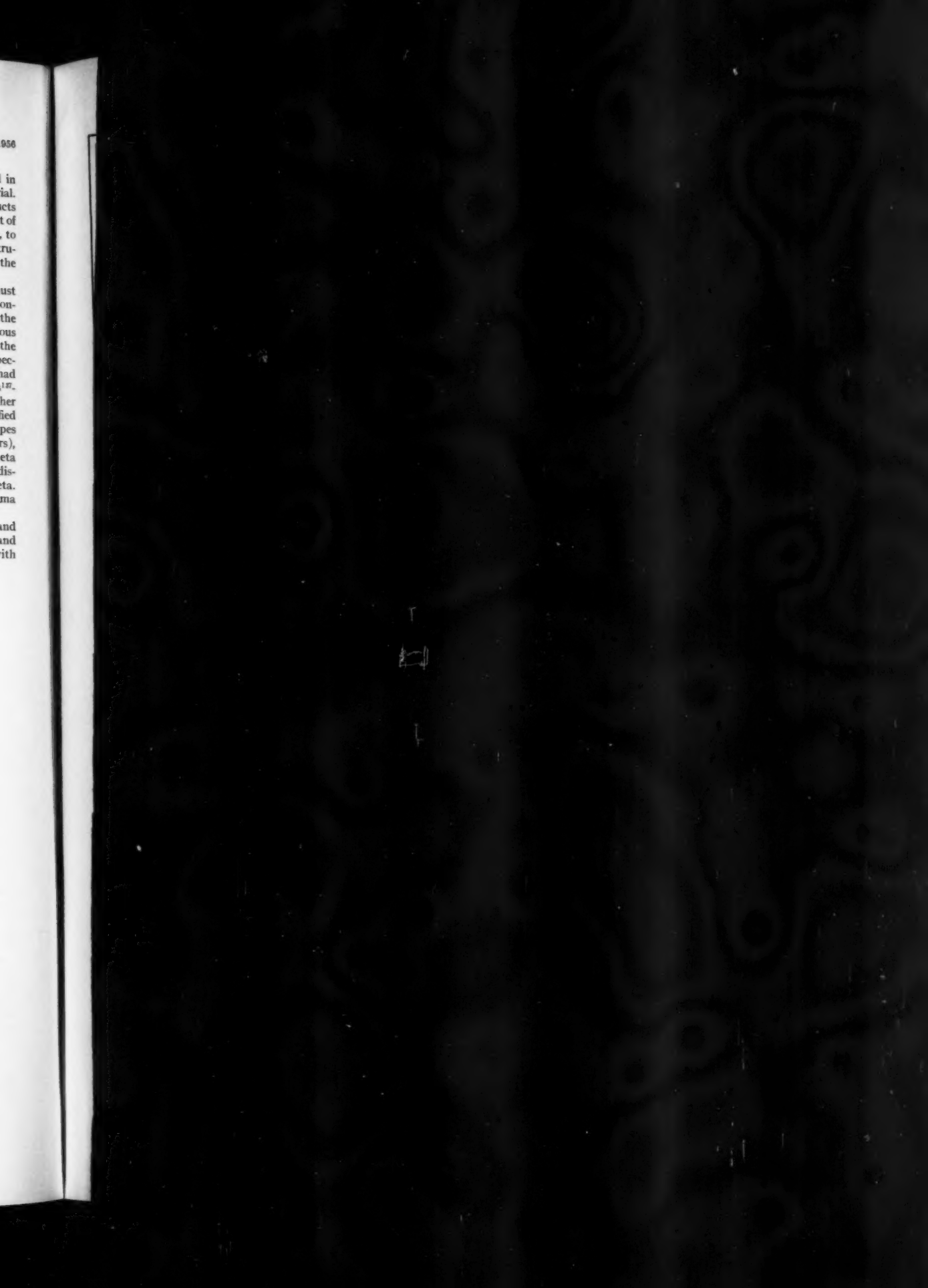
The authors present a very brief preliminary report on the protection of skin against radiation damage. Fifteen white rats were subjected to different doses of radiation on three separate skin areas and were variously fed. In 3 the diet consisted of 100 per cent spleen both before and after irradiation; 3 received 50 per cent spleen before and after irradiation; 3 were given 100 per cent and 3 50 per cent spleen preceding irradiation, with a normal diet afterward; 3 were on a normal diet throughout the experiment.

The skin of the rats receiving spleen (100 per cent or 50 per cent) postirradiation was generally in better condition than in those given no spleen after irradiation. The most serious damage was observed when no spleen at all was given.

Estimation of Curie Content of Packaged Radioactive Wastes. Frederick B. Oleson. Arch. Indust. Health **12**: 383–387, October 1955.

At Brookhaven National Laboratory (Upton, Long Island, N. Y.), solid radioactive wastes are packed in concrete-lined 55-gallon steel barrels for sea burial. Most of the activity comes from mixed fission products over one year old. In order to determine the amount of activity thus disposed of, it is necessary, in practice, to relate the mr/hr. readings of gamma survey instruments at a specified distance from the barrels to the activity in curies.

To make this relationship quantitative, one must obtain a known amount of the activity in highly concentrated liquid form and make a measurement of the r/hr. per curie of total activity at 1 foot for various thicknesses of the concrete lining. An analysis of the gamma-ray energy spectrum with a gray-wedge spectrometer showed that 95 per cent of the gammas had an energy of 0.66 MEV. This was attributed to Cs^{137}-Ba^{137} (33 years) in the mixture. The fact that other gamma energies were not significantly present simplified the problem. On theoretical grounds, other isotopes present, such as $Sr\text{-}Y^{90}$ (25 years) and Pm^{147} (3.7 years), have very simple decay schemes and are pure beta emitters. Thus, it could be shown that every disintegration was accompanied by a detectable beta. The beta activity was approximately twice the gamma activity.

The effective absorption coefficient of ordinary and heavy concrete in the cylindrical geometry for Co^{60} and methods for estimating the activity of material with Co^{60} contamination are discussed.

Four figures; 3 tables.